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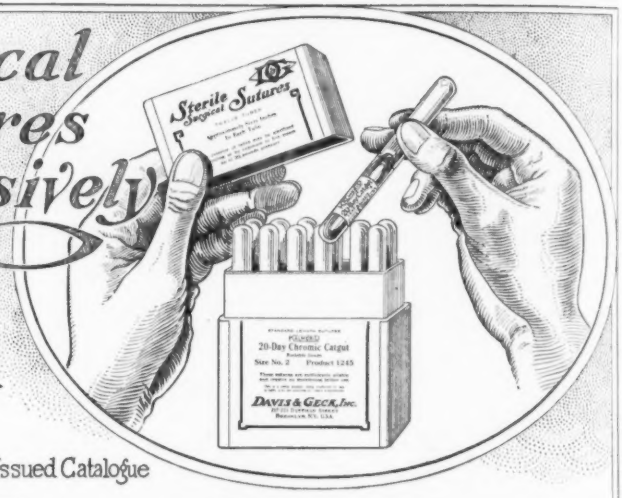

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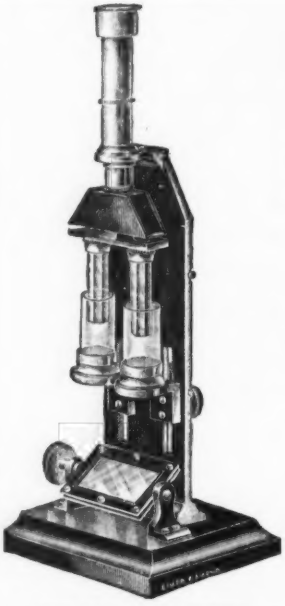

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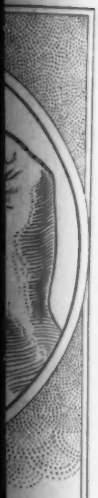

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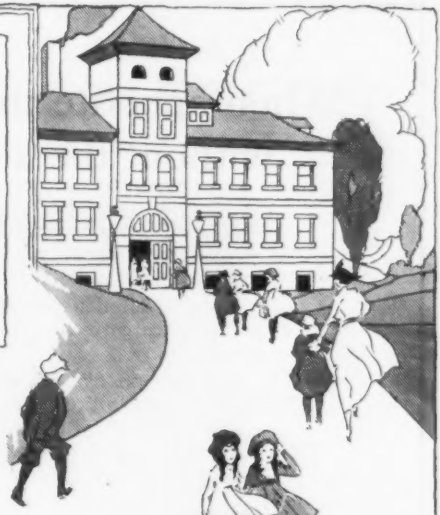

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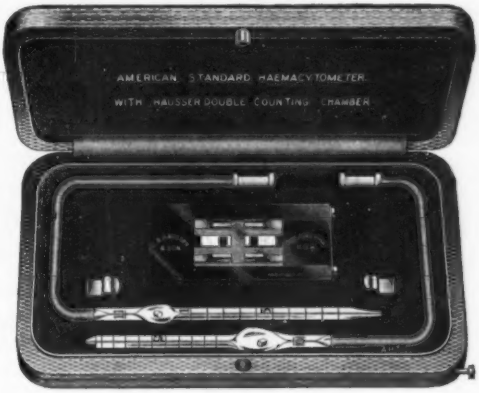

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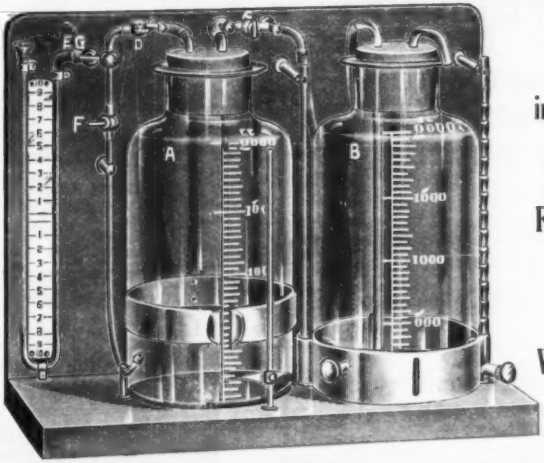

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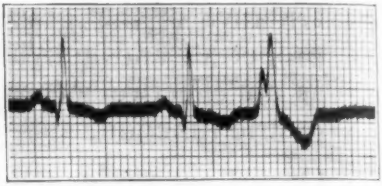

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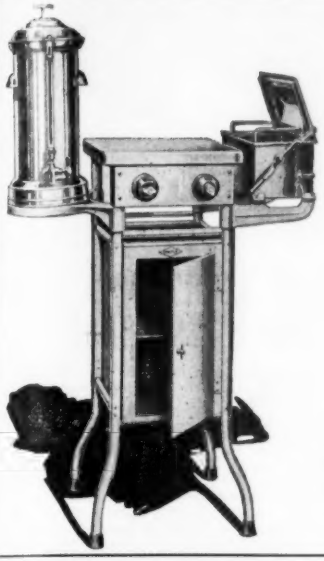

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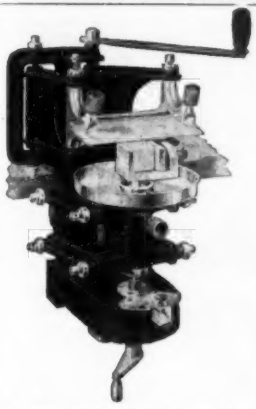

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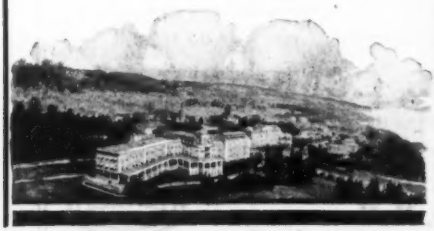

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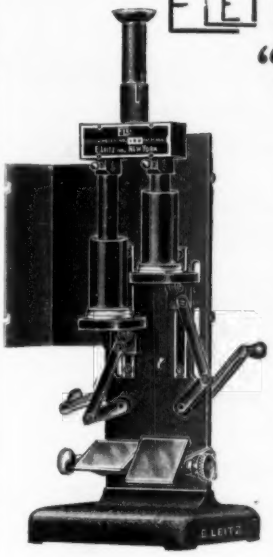

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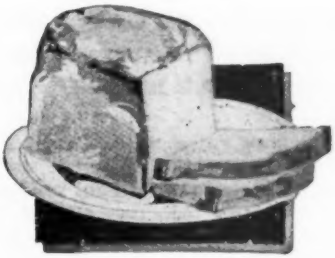

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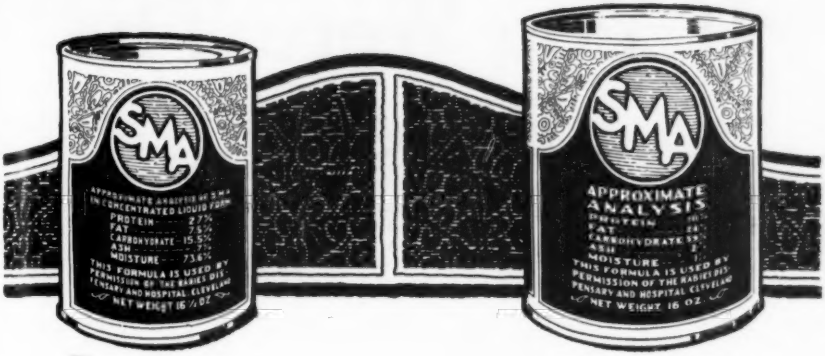

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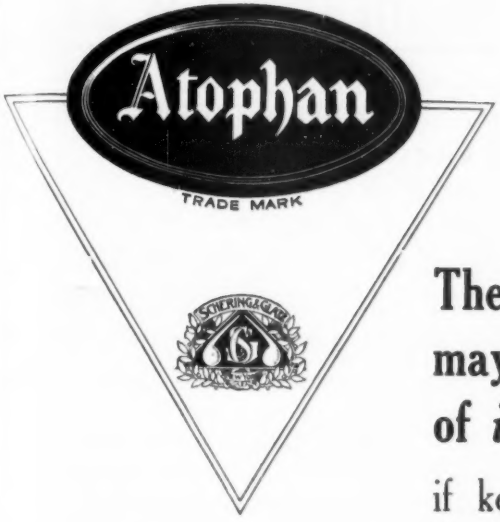

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OF THE MEDICAL SCIENCES

SEPTEMBER, 1922

ORIGINAL ARTICLES.

INFECTION OF THE GASTROINTESTINAL TRACT IN SYSTEMIC DISORDERS:

Medical Viewpoint with Special Reference to Classification of Cases; the Importance of Advanced Bacteriology and Biochemistry.*

By G. Reese Satterlee, M.D.

NEW YORK.

There is no such thing as a "medical case" in gastrointestinal diseases. Every patient should be studied by the internist and surgeon conjointly. Most cases need minor surgery of some sort, but few need major abdominal operations. Infection plays an important role in every case. The profession is fortunately awakening to the necessity of a very complete survey of every chronic intestinal invalid. Without this thorough study, reports and statistics are without value. In the past, and still unfortunately in the present, many an abdominal operation for gall-bladder disease, stomach or intestinal ulcers, adhesions, chronic appendicitis, bowel resections and exclusions has had bad sequelæ or at least disappointing results. The reason for this has been due, in numerous instances, to overlooked focal infections or to a disregard to the fact that the abdominal pathology may itself constitute a focal infection and require further investigation.

It has long been known that mouth disease breeds stomach and intestinal disorders, but in spite of this fact the mouth has

* Read before the New York County Medical Society, at the New York Academy of Medicine, December 23, 1921.

been constantly neglected as an important factor in these ailments. The tendency is quite general to regard the mouth as of secondary importance. Even if so considered it must be conceded that focal infections in the mouth or elsewhere may be a detriment to health and should be thoroughly removed. It is our opinion that these focal infections should be removed when practicable, prior to abdominal operation.

The study of the morphology and function of the gastrointestinal tract has made very rapid strides during the past few years. It is now regarded as a routine procedure always to be employed in the investigation of a chronic digestive disorder, no matter how simple the conditions may appear. Morphologic defects in the gastrointestinal tract should be studied from the bacteriologic standpoint. When the stomach or duodenum are involved, cultures from contents removed through the duodenal tube, according to the fractional analysis method, are frequently of value, not alone for diagnosis but for vaccine therapy. Cotton and Satterlee[1] have noted the high bacterial content in gastric contents that are deficient in free hydrochloric acid and also the converse. After a course in autogenous vaccine or serum therapy, the gastric contents have in many instances returned to normal. It is probable that gastric infection has been responsible for the abnormal gastric contents. Our results have made us believe that the bacteria recovered in this way may not be accidental although the method of obtaining the bacteria is necessarily open to criticism.

A large number of causes of gastric and duodenal ulcer are given, Smithies[2] cites 10 causes in 522 cases of proved gastric ulcer. In his list of causes he places only 33.1 per cent under the head of acute and chronic infections. However, it seems reasonable to suppose that there is present infection in the ulcer, at least as a secondary occurrence. Smithies recognizes this. Until we have more definite information as to the origin of these ulcers, we must be contented in dealing with them as terminal affairs in the hope of curing them as such with little chance of prevention.

The Medical Treatment of Chronic Intestinal Toxemia. This consists of diet, massage, hydrotherapy and vaccines or serum.

The diet consists of animal protein free food, principally vegetables, fruit and cereals.

Refined white flour is eliminated and whole wheat flour substituted.

The diet at first is very strict; no eggs and very little milk being allowed.

Bran is an essential article and is given once or twice daily—1 to 2 ounces.

[1] Fractional Gastric Analysis, Tr. Section on Gastroenterology and Proctology, Jour. Am. Med. Assn., 1920, **29.**

[2] Jour. Am. Med. Assn., 1920, **74,** 1555.

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When the stools are dry and hard, agar is given in the food. A liberal diet is permitted and encouraged, but it is often wise to underfeed rather than overfeed.

All laxatives and cathartics are forbidden. This includes mineral oil. Caster oil is useful occasionally when specially indicated, but only under special instructions. The same is true of enemata and colon irrigations.

Continued use of drugs and irrigations is harmful. Colon massage is of great value in obstinate constipation. Its use should be systematic.

Hydrotherapy, in the shape of eliminating cabinet baths, followed by Scot's douche helps the physical welfare of the patient.

Electrotherapy and mechanotherapy are also of great value, provided the patient can afford the time.

Vaccines and Serotherapy. It must be constantly borne in mind that the constipation in most of these cases is of toxic origin, probably protective. It is possibly for this reason that laxatives and cathartics are harmful.

It is with this idea in mind that we have practised vaccine and serotherapy in nearly all our suitable cases, and with satisfactory results. Dr. Cotton has found that vaccines and sera are important aids in the treatment of toxic psychoses, both before and after operation. He and the writer[3] practised successfully along these lines before knowing of the other's results. We also had many satisfactory results with the vaccines alone before becoming convinced of the necessity of removing all obvious foci of infection.

The routine procedure for colon vaccines is to obtain the stool after a purgative dose of castor oil. The third stool is preferable, as it contains the virile bacilli from the ceco-colon region. Cultures are taken and a vaccine made from the isolated colon organisms by the usual well-known technic. These vaccines are given as a routine every four days in doses of from 100,000,000 to 300,000,000, depending upon the general reactions. The duration of treatment depends upon the degree of immunity established in the individual case.

Serum Therapy. We owe the serum to Dr. Cotton's researches. It is obtained from a horse that has been immunized by the various strains of streptococci and colon bacilli obtained from cultures from infective foci in the patients at the New Jersey State Hospital.

My own results with this serum have been very gratifying in the few cases in which it has been used. The dosage begins at 1 cc and gradually increases up to the full dose of 10 cc.

The one disadvantage of the serum is the occasional occurrence of serum sickness. The intestinal toxic symptoms subside rapidly after its administration.

[3] Satterlee, G. R.: New York Med. Jour., 1918, **107**, 971.

Of other therapeutic agents generally employed there is little to recommend. Lactic acid cultures are of little value. Bulgarian bacillary milk has the value of a good milk food and may be of service in some cases.

Saline cathartics are harmful. The intestinal antiseptic drugs recommended, such as salol, creosote, etc., may be of temporary value, but symptomatically alone. Antacids and acids are often necessary and valuable aids, but in final analysis materia medica falls down as a curative agent.

Metabolic studies are essential in some patients in which disorders in metabolism are suspected. The diet should be modified to suit the case.

Infections with their consequent toxemias play the important role in most disorders of the alimentary canal.

If Rosenow's[4] work on the experimental production of gastric and duodenal ulcers following the injection into animals of bacteria derived from cultures from the apices of infected teeth, thereby demonstrating the selective action of bacteria, is as accurate as it appears to be, the value of preventive dental surgery will have been established. Bumpus and Meisser[5] have recently produced in animals streptococcic kidney lesions from cultures obtained from apices of devitalized teeth in patients showing pyelitis at necropsy. Our clinical experience seems quite in sympathy with this theory of the selective action of bacteria, so much so that we use it as a working premise. This lead follows directly into a most important field, that of *preventive surgery of the mouth*. This new and important branch of preventive medicine is still in the experimental stage, and after the necessary adjustments which will follow upon its extended clinical use, will in our opinion, prove to be of very great value. The question of the day is, "Should this problem be left alone to the laboratory worker or developed both clinically and experimentally? Should we leave these badly necrotic areas alone if no local or positive systemic symptoms exist or should we interfere?"

There is great need for more experimental work, and especially for *coöperation* between the oral surgeon, the dentist, the physician and the surgeon.

The bacteriology of dental and oral infections is studied in the laboratory of our office, cultures being taken from the apices of extracted teeth, necrotic bone areas and opened antra and from all tonsillar tissue removed. The technic employed is that of Holman.[6]

The all-important question relates to the effect of these hidden

[4] Jour. Infect. Dis., 1915, **17**, 219.
[5] Jour. Am. Med. Assn., 1921, **77**, 1466–1468.
[6] The Classification of Streptococcus, Jour. Med. Research, 1916, **34**, 377.

chronic infections upon the general mental and bodily condition and on the gastrointestinal tract.

There is every reason to consider the gastrointestinal tract from the lips to the anus as one organ, the structure, development and function being correlated in the closest possible manner. Foci of infection in the mouth or in the rectum frequently give rise to a similar train of symptoms, the predominating ones being constipation and flatulence. The removal of these obvious foci, provided the remainder of the tract is free from focal infection or permanent changes, will frequently clear up the intestinal symptoms and restore, without further intervention, the physical and mental equilibrium.

It is unfortunate, however, that patients are not studied in many instances before the infection has progressed to the stage of gastrointestinal ulcers, gall-bladder disease and permanent changes in the colon, when major instead of minor mutilation is definitely indicated—often with poor results. It is not amiss to speak here of our experience in chronic appendicitis. In a previous paper by one of our group (Satterlee[7]) 25 per cent of the patients with diseased colon had had the appendix previously removed without benefit or with apparent detriment. It is difficult to say just what this means. We incline strongly to the belief that often the primary infection was oral and that by the time the appendix was removed the toxemia had become generalized. When this had taken place the patient's condition was involved and the chances of cure more remote than in the early stages.

From a detailed study of over 1000 chronic intestinal invalids medically treated and of over 200 similar patients in whom a portion or all of the colon had been removed, we have come to the belief that many of these advanced cases with infected colons will not get well until the diseased portion of the organ is removed together with every other local focus. Medical treatment with vaccines and sera is indicated in every case.

The sequence in infective processes of the gastrointestinal tract is difficult to follow and to explain. The infection must travel in one or more of three ways: In the blood stream, lymphatics or lumen of the gut. Our operative experience combined with pathologic and bacteriologic findings leads us to believe that infection from the ceco-colon reaches the body cavity *via* the lymphatics, as evidenced by the enlarged lymph nodes in the mesentery. Colon bacilli and streptococci are frequently obtained from cultures of these nodes. Many observers consider that infections of the kidneys and other parts of the urinary tract originate in this manner.

The protective lymphatic system acts as a barrier to bacteriemia from these organisms, many of which are very pathogenic.

[7] Chronic Appendicitis and Chronic Intestinal Toxemia, New York, Med. Jour., 1916, **104**, 882.

Chronic intestinal invalids, therefore do not suffer from a bacteremia but from a *toxemia*. This debilitates and deteriorates but rarely kills the patient directly. The human system may, under these toxic influences, undergo a lowering of resistance and become susceptible to other and perhaps more lethal infections.

It has become my fixed belief from prolonged study of chronic intestinal toxemia that the colon bacillus, perhaps the pathogenic forms only, is the primary cause of this lowered resistance, and that other types of bacteria, notably the streptococcus, are secondary infections. On the other hand, Bumpus and Meisser, in describing infection of the kidney by the colon bacillus, have suggested that the primary cause of this infection may be streptococci carried to the kidney from the colon through the lymphatics and that the colon bacilli as a secondary implantation have overgrown and supplanted the former. Much more study in the line of clinical research and experimentation is needed in this direction.

My own view of this subject is based on the study of over 500 cases of chronic intestinal toxemia treated by autogenous colon vaccines obtained from stools after catharsis. A suitable case, one with symptoms and signs of a chronically diseased ceco-colon, will invariably improve after the administration of autogenous colon vaccines, and also, as we have discovered lately, of an anti-colon and antistreptococcus serum prepared under the direction of Dr. Cotton. The reason for this improvement is, I believe, that the resistance of the individual has been enhansed.

As students of intestinal pathology it has been our misfortune that up to the last three years insufficient attention has been paid to the study and eradication of foci in all other parts of the body. The principal locations of these foci are in the tonsils, teeth, abscesses and necroses in the jaw, in the nasal sinuses, rectum, seminal vesicles and cervix uteri. Some of our former patients, who had been improved but not cured by vaccines and general medical therapy or by resection of the right colon, have since been restored to efficiency after the removal of these obvious foci of infection.

These principles are applicable to other diseased conditions, as, for example, in syphilis. Cotton[8] has observed chronic cases that could not be improved until the obvious foci of bacterial infection were removed. This has been my own experience in a limited number of cases. I will cite one case as an example: Male, aged forty years, with tertiary lues untreated for several years, severely affecting the heart, aorta and liver. After four years of the usual antiluetic treatment he improved but still showed a four-plus Wassermann and other signs of luetic activity. This year, after removal of an extensive mouth and jaw infection, with-

[8] Personal Communication.

out further antisyphilitic treatment, the Wassermann dropped to one-plus with other corresponding signs of improvement.

One of the most puzzling aspects of gastrointestinal infection is that it may produce the most profound mental or nervous disturbance, with little or no direct gastrointestinal symptomatology. Attention was called to this by one of our group (Satterlee[9]) in 1917. Careful neurologic study of these patients will reveal no etiologic factor until a detailed and complete study of the gastrointestinal tract and a thorough search for foci in other parts of the body have been made. Eradication of the diseased areas has brought about a return to normal or a great improvement, provided that deterioration has not progressed too far.

In this age of progress a single track is to be avoided and all our faculties must be used in thorough investigation, followed, if justified, by equally thorough treatment.

CULTURES FROM APICES OF EXTRACTED TEETH

Streptococcus mitis recovered in 37 extracted teeth.
Streptococcus salivarius recovered in 24 extracted teeth.
Streptococcus anginosus recovered in 7 extracted teeth.
Streptococcus pyogenes recovered in 6 extracted teeth.
Streptococcus equinus recovered in 4 extracted teeth.
Streptococcus fecalis recovered in 3 extracted teeth.
Staphylococcus albus recovered in 23 extracted teeth.
Staphylococcus aureus recovered in 4 extracted teeth.

Of the streptococci, the streptococcus anginosus and pyogenes are of the pathogenic hemolytic type, the others—mitis, salivarius, fecalis and equinus—are non-hemolytic.

CULTURES FROM NECROTIC BONE AREAS

Streptococcus mitis recovered in 13 cultures.
Streptococcus salivarius recovered in 9 cultures.
Streptococcus anginosus recovered in 6 cultures.
Streptococcus pyogenes recovered in 3 cultures.
Streptococcus equinus recovered in 2 cultures.
Streptococcus fecalis recovered in 1 culture.
Staphylococcus albus recovered in 8 cultures.
Staphylococcus aureus recovered in 1 culture.
No growth recovered in 11 cultures.

Contamination in 1 culture.

It is thus to be noted that in 80 cases in which dental extraction and bone operation were performed the most frequent streptococcic

[9] Jour. Am. Med. Assn., 1917, **69**, 1414–1417.

organisms recovered were from the apices and bone, the streptococcus mitis and salivarius of non-hemolytic type. Next the Streptococcus anginosus and pyogenes of the hemolytic type. The Streptococcus subacidus and equi have not as yet been found from our cases.

In analyzing the physical condition of the patients under treatment no conclusions in reference to the type of the organism recovered and the severity of the symptoms can, as yet be drawn.

Where the hemolytic organisms were recovered with one exception, the patients were distinctly ill. In one patient (M. J. C.), where all of the streptococcus organisms except the streptococcus fecalis, subacidus and equinus were recovered, marked cervical adenitis of persistent character was present.

CULTURES FROM ANTRA DIRECTLY ON OPENING THROUGH THE MOUTH

Streptococcus mitis, 12	Staphylococcus albus 21
Streptococcus salivarius, 9	Staphylococcus areus 3
Streptococcus anginosus, 3	Mucosus capsulatus, 1
Streptococcus pyogenes, 5	

These results correspond quite closely to the cultures from the teeth and bone cultures.

CASE I.—A. F., male, aged sixty-one years, retired business man.

Chief Complaint. Blood in the urine for twenty years, with occasionaly severe hemorrhages. Renal calculus passed at the ages of twenty-four and forty-four, also gravel at times. Nervous depression and inability to work.

Diagnosis. Chronic intestinal invalidism with secondary renal involvement.

Past History. Scarlet fever twice, at sixteen and twenty-nine years. Slight deafness following otitis media in the right ear. Severe attacks of asthma every summer. Chronic digestive disturbance. Could not carry a light suit-case without a tight abdominal belt.

Family History. Brother has had occasional blood in urine.

Examination. Enteroptosis, including kidneys, three-plus; nutrition poor. Blood coagulation four minutes. Roentgen-ray demonstrated, no renal calculi. Infected teeth with necrosis and infected antrum. Ureteral catheterization showed red blood cells and occasional leukocytes from both ureters and 18 and 13 per cent of phenolsulphonephthalein in four minutes from the left and right kidneys respectively. Cultures from ureters showed Bacillus communior from both sides. Dental extraction and removal of necrotic areas and drainage of antrum done. Strepto-

coccus mitis and salivarius recovered. Vaccines made from the above colon bacillus isolated by ureteral catheterization administered over a period of six months.

Results. Excellent. General condition markedly improved. Patient can play thirty-six holes of golf without fatigue. One slight attack of blood in the urine during vacation when vaccines had been suspended. No attack of asthma this year. Urine examination six months after vaccine treatment began showed no red blood cells and no colon bacilli. Patient has not had so prolonged a period of well-being without hematuria for years.

This case is very suggestive of the connection between oral infection and kidney lesions. It is of speculative interest as to the relationship of the streptococci and the colon bacillus in kidney infections, especially those accompamied by hematuria.

CASE II.—S. F. B., female, aged fifty-four years.

Symptoms. Periodic attacks of loss of appetite; "bilious attacks;" "indigestion;" disgust for food and long periods of self-inflicted starvation. Spasm of esophagus on one occasion. Attacks of diarrhea with severe mental depression. Constipation habitual up to two years ago. Medical treatment for hemorrhoids, flatulence and nervous headaches for the past four years. No improvement. Pronounced neurasthenia and hypochondria; irascibility; incoöperative, incompetent, bordering on severe mental derangement. In bed most of the time.

Examination. Emaciated, anxious, sallow patient. Extensive fixed bridgework. Numerous capped and crowned teeth. Infected tonsils; hemorrhoids; femoral hernia (reducible). Hemoglobin, 70 per cent, white blood cells, 10,000. Gastric fractional test, 18 per cent subnormal. Mucus 2-plus. Extreme nervous debility.

1. *Dental Operation.* September 26, 1921. Seven teeth removed. All necrotic bone, including floors of both antra, removed. Follicular cysts in the molar areas. Bone necrosis from the roots extended back to the palatal portion of the superior maxilla and to the first bicuspid on the upper right side. In the left antrum there was a catarrhal condition on the nasal side of the antrum opening into the nasal passage. Two openings from the necrosed areas into the nasal passage. Marked improvement.

2. *Tonsillectomy.* Marked improvement.

3. *Hemorrhoidectomy.* Removal of infected crypts. Still more improvement and physical strength greater than in the past three years. Also striking diminution of nervous and mental symptoms. Return of personality to normal.

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This case is one illustrative of marked nervous, mental and physical disorders improved by surgical treatment of certain foci, but not fully relieved until *all* foci had been removed. The improvement in physique and personality has been striking.

CASE III.—A J. LaC., female, aged fifty-two years. Teacher. Hemicrania; melancholia, suicidal. Progressive constipation for fifteen years. Blood-pressure averaging 235/150. Partial colectomy for diseased ceco-colon and obstructive adhesions in 1914. Marked betterment in mental and physical condition and able to carry on her work. Postoperative condition materially improved by enteroantigens (autogenous colon vaccines). Patient had some dental difficulties with occasional alveolar abscess, but no particular attention was paid to the teeth at the time, 1915-16. Fairly well until 1918, when she had another severe headache with high blood-pressure after extensive dental repair. The phenolsulphonephthalein output on various occasions was well above normal; this with chemical blood examinations demonstrated normal kidney function. In March, 1921, extensive infection in molar regions with necrosis and infected antrum. Operation, with marked general improvement, so that the patient is better today than she has been for over twenty years. Blood-pressure, July 20, 1921, 185/120. This case is typical of the value of the complete removal of all focal infection as early as possible.

INFECTION OF GASTROINTESTINAL TRACT IN RELATION TO SYSTEMIC DISORDERS:

SURGICAL VIEWPOINT: COLECTOMY; INDICATIONS, PATHOLOGY, TECHNIC, MORTALITY.*

BY JOHN W. DRAPER, M.D.
NEW YORK.

FROM the standpoint of infection of the gastrointestinal tract, that portion of greatest interest in surgical research is necessarily the colon. This terminal portion of the bowel is of much less vital need to the organism than the central portion; it is frequently diseased and can be dispensed with, entirely or in part, both in human beings and in the lower vertebrates. The entire problem is thus one of engrossing interest to the specialist and to the general practitioner alike.

* Read before the New York County Medical Society, at its stated meeting, Academy of Medicine, December 23, 1921.

The similarity between the stomach and the colon has often been noted, particularly as regards their functions, those of storage and motility far outweighing in importance all others. After removal of the stomach in the lower vertebrates, and in man, it has been found that all of its subsidiary functions, as well, apparently, as the two major ones just named, are taken on vicariously by other portions of the tract or indeed largely abrogated. The same is true of the colon. Between the stomach and the colon lies the small bowel, a relatively short portion of which is essential for life. Here, digestion and assimilation take place. Save for the correction of minor conditions, this portion of the alimentary canal is inviolate to surgical intervention, and one has only to initiate the simplest form of surgical research in this region to become convinced that the further invasion of this great laboratory of the body by surgical procedures is improbable.[1] [2] In a scholarly paper just published,[3] Eisberg has shown, by what seems to be the most conclusive proof, that the duodenum and the contiguous portion of the jejunum is one of the most highly specialized and least understood portions of the entire body, the beginning and end of the canal decreasing in specialized activity and in obstructive toxicity in a fixed ratio as one departs orally and aborally from the duodenojejunal junction. Why is this so? Why is not the alimentary canal bilaterally symmetrical like all the other great systems of the body? Why finally does the midpart of the canal remain free from disease, notably cancer and infection, while both ends are the frequent seat of malignancy and of bacterial invasion as well?

Is it not probable that the law of use and disuse is as applicable to the alimentary canal as elsewhere in Nature, and that we may properly seek an explanation therein for this well-known clinical fact, that the colon and stomach are more liable to degenerative changes than the rest of the alimentary canal? Closely coupled to this is the now universally admitted effect of gravity upon the development of colon pathology. These biologic and morphologic factors interact and favor at least partial explanations of the surgical findings. Moreover, it cannot be denied that, as Bryant[4] and other students of this matter have shown, men and women are clearly divisible into three definite types, one of which is distinctly unfavorable to the upright position, and from which many cases of chronic intestinal invalidism are recruited. It

[1] Frazier and Peet: Experimental Colonic Stasis, Ann. Surg., June, 1916, **63**, 729–731.

[2] Draper, John W.: Observations upon a Form of Death Resulting from Certain Operations on the Duodenum and Jejunum, Surg., Gynec. and Obst., 1906, **2**, 502–509.

[3] Experimental Intestinal Obstruction, Ann. Surg., 1921, **74**, 584–609.

[4] The Carniverous and Herbiverous Types in Man, Boston Med. and Surg. Jour., 1916, **174**, 412–416.

is evident that in the course of the adaptations, which were a necessary precedent to the upright position, many changes which would have been beneficial did not take place, and in this matter the colon has proved to be no exception.

In spite of much recently acquired information regarding the colon, notably the fact that even if not diseased its entire removal is compatible with the health, the growth and the development of the individual, its vital functions being apparently *nil*, it cannot be urged too strongly that the indications for its removal, either partial or complete, are rarely to be met with, most cases responding promptly to modern medical treatment. That, however, definite indications for total or partial colectomy are occasionally demonstrable is shown by the increasing literature on this very important subject. One of the most recent articles upon colon resection is that by J. Schoemaker,[5] of The Hague, Holland, who, speaking before the Clinical Congress of Surgeons at Philadelphia, stated that in no less than 179 cases, and with a loss of only 2 patients, he had removed the cecum, ascending colon and part of the transverse colon "in cases with pericolitis associated with obstipation." It is unfortunate that the brevity of this article precludes the further discussion of the indications which led him to the development of this remarkable series.

The subject of colon pathology, particularly in its relation to the etiology of systemic disorders, is at present little understood. This problem is beset with the greatest difficulties from the bacteriologic standpoint, and although much is known about the occurrence of colon lesions in individual cases, enough evidence is not yet available to prove that any particular group of mental symptoms can with certainty be attributed to a given colon pathology. Such evidence is, however, rapidly accumulating. For this very reason the record herewith presented of colon pathology found among 170 toxic psychotic patients at the State Hospital at Trenton is of the utmost importance. For it is only by an accumulation of a large amount of such material, by its careful correlation with all the symptomatology and by a postoperative survey of the patients extending over a number of years, that definite conclusions as to cause and effect can be reached.

Dr. John F. Anderson, who is in charge of the bacteriologic work at the State Hospital, and to whom we are indebted for constructive criticism in the interpretation of our surgical bacteriology, looks upon the problem of colonic infections as still unsolved, but as promising to contribute invaluable information when better understood. Dr. James Ewing's report, herewith appended, upon our specimens supports this position and is convincing, not alone of the extent of the pathology but of the indication for con-

[5] Some Technical Points in Abdominal Surgery, Surg., Gynec. and Obst., 1921, **33**, 591–596.

tinued study. Probably we shall have to wait for a further development of the theory of bacterial specificity before being able to obtain from the laboratory a final explanation of these phenomena.

Before considering a partial or total colectomy in any given instance, it is evident, therefore, that the indications—historical, physical and roentgen ray—must be particularly well defined. There must be a long-continued history of chronic intestinal invalidism, with its usual but not invariable evidence of chronic appendicitis early in life, with "bilious attacks" and "bellyaches," often with oral infections later on, with the occurrence of right-sided abdominal rigidity, and often with tenderness, pain and superficial hyperesthesia, always with colonic delay, defined and localized by roentgen-ray study. Even in the presence of such findings, surgical intervention is, in our opinion, not indicated except there be also well-defined and serious subjective symptoms. It is now eight years since, under the above conditions, our earliest prepsychotic cases were operated upon, and the continued study of these patients not only strengthens our belief in the very important relation of colonic infections to general health, but also affords interesting ground for belief that in many cases there are personality changes associated with chronic intestinal invalidism which may ultimately become fixed in character, constituting definite toxic psychosis. We have reported such changes in childhood and have urged prevention through the recognition and removal of physical causes.[6]

Every practitioner is familiar with the mental depressions which accompany intestinal invalidism, and many must have noted a gradual transition from ordinary depression, apathy and incoordination to well-defined insanity. Often there appears to be a definite gradation between the preinsane and the insane not hitherto recognized, and upon which Cotton's work at Trenton will cast light. Indeed, the establishment of such sequence, or gradation, among the mentally afflicted may prove to be one of the most important results of the development of his theory. Mutation from a simple depression to a definite psychosis certainly occurs with sufficient frequency to interest the general practitioner, and to add to his already great burdens that of early physical diagnosis as an aid to preventive psychiatry. Indeed, prevention is the keynote of the whole matter.

Finally, we feel that no patient should be subjected to colectomy for chronic intestinal toxemia except upon the collective decision of a medical group, it being, in spite of low mortality, a far too serious operation to be decided upon by one physician alone.

In the series herewith presented the evidence for operation based upon ample physical lesions has been augmented by the presence of a psychosis. This has helped to make the decision

[6] Draper, J. W.: Preventive Surgery, New Jersey State Jour. Med., January, 1922, **19**, 1–9.

to operate much easier because elective surgical procedures are more properly employed in patients presenting such serious subjective symptoms than otherwise.

The technic at the State Hospital at Trenton for total or partial colectomy is the direct outcome of the writer's experimental work in intestinal obstruction upon the lower vertebrates, so that for technic as well as for interpretation the present research is primarily indebted to the laboratory.[7]

Technic. The cecum is lifted mesiad by the assistant and the limiting pericolic membrane is cut with scissors. When this is done the ilecolic vessels are exposed. These are ligated with heavy linen. The right and midcolic vessels are ligated and the bowel is separated from its mesentery. If it has been decided to do a right-sided resection only, the ligation and cutting of the mesentery cease at this point and a heterostaltic lateral anastomosis is made. If the entire colon is to be removed the omentum is split at this point and ligated right and left. This liberates the mesentery and facillitates its ligation. If the splenic flexure is high it will often be necessary to cut across the left rectus muscle, preferably between the tenth and ninth nerves. The flexure should be put on traction mesiad, and the left pericolic membrane and phrenicocolic ligament, which are often fused, carefully separated with scissors points. It is extremely dangerous to make more than the most gentle traction at this point, as the colon is friable at the flexure. The mesentery of the descending colon and sigmoid is then separated as far as the lower sigmoid artery. It is important not to injure this. The patient is then put in the Trendelenburg position and the retroperitoneum is picked up by blunt artery forceps at intervals of about 2 cm. The peritoneum is then tied together, beginning at the bottom of the "U." This obliterates the space into which the bowel would fall between the cut mesentery of the ileum and the sigmoid, and avoids danger of obstruction. The bowel segment is then removed and the anastomosis made heterostaltic and lateral, this having been found to functionate as well as a prostaltic lateral, and end-to-side or an end-to-end anastomosis.

MORTALITY OF COLON RESECTIONS AT THE TRENTON STATE HOSPITAL

	Cases.	Deaths.	Per cent.
1919	34	13	40
1920	59	18	30
1921	77 (31 complete)	10	12
	170	41	24

[7] Draper, J. W.: Studies in Intestinal Obstruction, Jour. Am. Med. Assn., September 26, 1916, **67**, 1080–1082; Intestinal Obstruction, Complete and Incomplete, Jour. Am. Med. Assn., October 7, 1916, **69**, 1768–1771.

Decrease due to operating on less degenerated earlier cases in 1920 and in 1921, and in addition to this the employment of anti-colon and streptococcus serum before and after operation.

Conclusions. 1. Colectomy should never be considered until all other local foci have been removed and the patient thoroughly treated from a modern medical standpoint, especially with vaccines and sera.

2. Extensive colon pathology exists in 20 per cent of all so-called "functional" psychotics. Mental symptoms have been arrested in 28 per cent of these and improvement has occurred in a large percentage.

3. The mortality of partial (46) and total (31) colectomy in the past 77 consecutive cases at the State Hospital has been 12 per cent.

Report on Dr. Draper's Specimens of Colon and Ileum. By James Ewing, M.D. I have examined sixteen specimens of colon and ileum removed at operation. The great majority of the specimens show very definite gross anatomic lesions which have resulted from chronic intestinal stasis and the ensuing chronic catarrhal inflammation. In several cases the lesions are extremely marked, in many they are well marked, while in a few there are no definite changes that can be regarded as more than minimal variations from the normal.

The most marked and constant lesion is pigmentation of the mucosa, which has rendered the inner lining brownish or at times dark chocolate in color. This change is most marked in the cecum, diminishing toward the sigmoid, but often present throughout the specimen. Sections show the pigment to be lodged in large polyhedral cells, lying in the mucosa and at times in the epithelium. Pigmentation of the colon is fully recognized as a sign of chronic intestinal stasis and intoxication. It is sometimes associated with anemia and at times with severe and even fatal dystrophies of nervous and muscular systems.

Pouching of the intestinal wall amounting almost to hernial protrusions was observed in most of the cases. These pouches were from 1 to 2 cm. in depth. The wall of the pouches was generally thinned, sometimes very much thinned, and the mucosa at the bottom was generally eroded, sometimes ulcerated. Through such erosions and ulcerations it is obvious that absorption of fluids and bacteria readily occurred. The usual contents of these pouches must have been fecal matter, and it appears that such material must have been practically incarcerated and seldom emptied. About the lower end of the cecum the pouches were especially numerous and deep, and access to them was tortuous, especially when external adhesions held the wall of the colon fixed.

The outer surface of the colon over the pigmented, and especially over the pouched district, was generally the seat of a chronic productive inflammation with the formation of very numerous

small granules of vascular connective or denser fibrous tissue. This granular appearance was doubtless exaggerated by hardening in formalin.

The loose serous coverings of the colon generally appear as thin membranes extending from the gut over the mesentery. These coverings often showed diffuse opacity from thickening, abnormal bands and striæ, and occasionally definite cicatricial contractions. To what extent these changes were due to the conditions inside the gut it is difficult to say, but probably they were largely caused by the mucous membrane lesions.

The lymph nodes in the mesentery accompanying the specimens were not, as a rule, enlarged, and often they were small and difficult to find. Sections of the nodes showed no inflammatory reaction of definite importance. It was noted that the lymph follicles were generally invisible in the colon and were reduced to a trace in the sections. Well-formed, recognizable Peyer's patches were not found in any case. There was therefore a general atrophy of the lymphoid apparatus inside and outside of the gut. That bacteria were found by culture in the lymph nodes of the mesentery could have been confidently predicted on the lesions of the mucosa and the lymphoid atrophy.

In general the impression gained from the study of these specimens was that the clinicians were dealing with extensive and somewhat unusual grades of chronic intestinal stasis and catarrhal inflammation with its sequels. In a few cases the conditions were such as to be practically irremediable except by mechanical straightening of the intestinal lumen. Whether or not extirpation of the cecum is the most direct method of accomplishing this object must be a matter of surgical judgment.

In perhaps the majority of the cases, and certainly in some, the conditions were not so advanced that emptying of the colon was impossible by lavage or frequent catharsis. Here, again the choice of methods must be regarded as a matter of clinical judgment. As for the specimens of ileum submitted, they failed to show any lesions that would necessarily call for extirpation. The indications for this procedure must rest entirely on clinical grounds.

The isolation of various bacteria from the mesenteric lymph nodes does not appear to have particular significance, since bacteria pass the relatively intact intestinal wall under a great variety of pathologic conditions, many of which have no connection with the clinical state of these patients. More important is the demonstration of hernias, pouching, thinning of wall, pigmentation and ulceration of the mucosa, which together form an impressive anatomic basis for the theory of intestinal intoxication, which undoubtedly existed in severe degree in the cases exhibiting such lesions.

Finally, I would venture to express my personal opinion that extirpation of the affected portions of the cecum and colon was justifiable and probably the only effective means of relieving the condition found in the advanced cases, while in others with slight changes the condition could have been met by less radical means. The extirpation of considerable portions of the ileum appears to me unwarranted if based solely on the anatomic condition of this organ.

INFECTION OF THE GASTROINTESTINAL TRACT IN RELATION TO SYSTEMIC DISORDERS.

Neurological Viewpoint; Special Relation of Clinical Symptoms to Regional Distribution of Focal Infection.

By Henry A. Cotton, M.D.

Trenton, N. J.

In presenting a psychiatrist's viewpoint of the relation of focal infections to systemic disorders before an audience of general practitioners, one must at the outset disabuse the mind of the physician of the timeworn traditional theories regarding the psychoses. Heretofore cases suffering from mental disorders were viewed with alarm by the general practitioner, through no fault of his own, however. The psychoses were elevated to a plane far beyond the vision of the physician. The symptoms were not understood and he felt helpless. The natural outcome of this situation was that psychotic patients were immediately committed to an institution for the insane.

This situation arose largely from our previous lack of knowledge of the causes of the various psychoses, and consequently there was no adequate treatment which could be instituted in the early stages of the mental disorder. Our fundamental knowledge of the psychoses has been based largely on speculation and coincidence, and the causes of the mental disorders were rather obscure and therefore no specific treatment could be instituted.

One of the most prevalent errors as to the causation is that of heredity. So fixed has this become in the minds of the profession and laity, and I might add psychiatrists as well, that it has been considered the principal, if not the fundamental, cause of the psychoses. This fact arose from the rather loose way in which records of heredity were gathered in the old state hospital statistics. Any patient in which there was "insanity in the family" was

noted as suffering from a hereditary taint. This occurred in sufficient numbers to substantiate the opinion that the psychoses were hereditary in origin.

It is needless to go into the various arguments from a biologic standpoint to show that this theory is erroneous. Not only were we in serious error regarding heredity, but such a doctrine was extremely fatalistic. For if a patient was born with the potential elements of mental disorder, then there was little use in trying to prevent the pyschosis or to successfully arrest it if it had appeared. Hence, the attitude was adopted that only by methods of training, education and favorable environment could these symptoms be forestalled. But we have seen many cases in which the environment was extremely favorable to the individual, where education and training were all that could be desired, and, in spite of this, psychoses developed.

In spite of the fact that perhaps 70 per cent of our patients give a history of "insanity in the family," especially in the institutional types, largely of the indigent class, there still remains a large percentage in which no hereditary taint can be discovered. The result of some five years' intensive study of the hereditary factors in the psychoses led the writer to a certain degree of skepticism regarding the importance of this factor, and today, while we do not eliminate the influence of an hereditary taint and its consequent inherited predisposition entirely, at the same time we are of the opinion that heredity should not occupy the exalted position it has previously held. As it has no bearing on the prognosis of a given case we believe that discussion is at present merely academic.

Psychogenic Factors. For many years the psychiatrists, in common with the profession at large, voiced the opinion that the psychoses were purely mental disorders caused by hereditary instability, plus psychogenic or mental factors. The physical condition of the patient was absolutely neglected, and our attention was centered alone on the psychogenic factors and the mental symptoms. This gave rise to a fundamental error in that we assumed the psychoses to be diseases of the mind caused by mental factors almost exclusively.

As no demonstrable lesions had been found in the brain cortex, it was considered that these disorders were "purely functional"—in other words that the disease of the mind was independent of any pathologic changes in the brain tissue. With an improvement in the methods of studying brain tissue and the results of our work the last four years, we have slowly arrived at the conclusion that the so-called functional psychoses were in reality caused primarily by disease of the brain and not of the mind, and that the mental disorders were merely symptoms of a diseased brain. The writer, working under Alzheimer in 1905-1906, produced conclusive evidence that there were changes in the nerve cells of

the so-called functional disorders, and this laid the groundwork for the future development of the idea that we must look to the anatomic lesions in the brain if we were to successfully arrest the psychoses, and, which is still more important, prevent them in time.

We would emphasize the fact that we do not minimize the importance of the psychogenic factors in precipitating a psychosis as we see a certain proportion of our cases in which such psychogenic factors as grief, worry, anxiety, shock and a host of others are present and undoubtedly play an important role in precipitating the psychosis. However, we have observed many cases in which these psychogenic factors are entirely absent. Hence, we have been forced to conclude that these factors, as in the case of heredity, play an important, but not the most important role, in the causation of the psychoses of the "functional" types.

Infection. If then we have destroyed our belief in the important role of heredity and psychogenic factors, what have we to offer in their place as causative factors? Formerly the physical condition of the patient was of minor consideration and many patients were classed as physically normal, which practice we know now was a serious error. We are indebted to modern mental practice for the methods which permit the finding of serious physical disease in apparently otherwise healthy individuals. The work of Billings, Hastings, Rosenow, Barker and Upson of the medical as well as Thoma and others of the dental profession has established, without any question of doubt, the doctrine of focal or masked infections. These infections were formerly overlooked not only in the psychotic patient but in patients suffering from various systemic disorders. This doctrine has been the most important contribution of twentieth century medicine and the application of the methods evolved to determine the presence of chronic infection has added an entirely new chapter to the treatment and prevention of the psychoses.

That local foci of infection which give no local symptoms and of which the patient may be ignorant can cause serious systemic diseases, both by spread of the organisms to other parts of the body and by a dissemination through the blood streams of the toxic products, the result of such infection, is still doubted by many; but we feel that enough work has been done to establish such a doctrine in spite of this skepticism.

Our investigations in the last four years have shown conclusively that the psychotic individual harbors multiple foci of infection which often can be located and eliminated only with the greatest difficulty and persistence on the part of the physician. In order to properly locate and eliminate these multiple foci of infection the psychiatrist has had to call to his assistance the specialist in other branches of medicine. So that today a well-equipped clinic for nervous and mental disorders is only adequate in so far as this principle of group diagnosis is carried out. The growth

of the idea of a diagnostic survey of every individual, whether suffering from mental disorder or other systemic diseases, has been rapid. One need only to mention the success of the Mayo Clinic and of the work of Lewellys Barker at Johns Hopkins to illustrate the trend of modern medicine. Why then should there be any criticism if the psychotic individual is given the advantage of the application of the principles of modern progressive medicine? In view of the successful application of these principles at the State Hospital at Trenton in the last four years, shall we still adhere to the old ideas expressed at the beginning of this paper, or shall we lay prejudice aside which limited the treatment of the psychoses to psychotherapy or the so-called occupational therapy and study the individual as a whole and endeavor to discover any pathologic condition which might be present?

It is only within the writer's short experience of twenty-one years that the question of the relation of syphilis to paresis was doubted in America. Paresis was considered a disease due to overwork, or mental strain, because it occurred in brokers, bankers, actors, and others who were supposed to be overworked. It was considered purely a mental disease. First a history of previous syphilis in a large proportion of the cases gave a clue to a better understanding of the causation. Then the studies of the brain cortex by Nissl and Alzheimer revealed the fact that very serious pathologic changes had occurred. Finally Moore and Noguchi demonstrated the Spirocheta pallida in the brain tissue in cases dying of paresis. Here we have an example where, step by step, our ideas regarding the causation of paresis underwent a complete revolution and no one would dispute the fact today that paresis is an organic brain disease due to destruction of the brain tissue by the Spirocheta pallida.

The so-called functional psychoses we believe today to be due to a combination of many factors, but the most constant one is the intracerebral, biochemical and cellular disturbance arising from circulatory toxins originating in chronic foci of infection situated anywhere throughout the body and probably secondary disturbances of the endocrine system. The psychoses then, instead of being considered a disease entity, should be considered as a *symptom*, and often a *terminal symptom*, of a long-continued masked infection, the toxemia of which acts directly on the brain. As psychiatrists have for years recognized a toxic infectious psychosis, especially in patients who had an obvious infection, acute in character and easily diagnosed, we have not established a new principle when we speak of the toxic origin of some psychoses. But we have extended the diagnosis to include types such as manic-depressive insanity, dementia precox, paranoid condition, etc., in which the infection is not apparent or easily found upon causal

examination. But such infection is only found upon utilizing all the methods of modern diagnosis, so it should not be difficult to adjust our ideas to these views.

If the profession at large can accept this viewpoint, which we feel we have demonstrated beyond a reasonable doubt, then their attitude will be changed from a hopeless, fatalistic one, previously in vogue, to a hopeful one wherein they themselves cannot only arrest many cases after a psychoses has developed, but, better still, by eliminating these foci of infection easily prevent the occurence of the psychose. There can be no question that many of the psychoses can and will be prevented when the result of such infection is properly understood by the profession at large. It is obvious that when the pyschoses can be arrested by eliminating chronic foci of infection, then by properly treating such patients long before the psychoses appears the mental disorder can be prevented.

Source of Infection. We have found that the source and type of chronic infection in the psychotic patient is the same as found in many of the systemic disorders. We may be pardoned, perhaps, if we claim that our work in the elimination of focal infection has gone further than in most clinics. We have utilized what we consider the best methods that have been developed. Some of them, unfortunately, are not in general use, nevertheless we are of the opinion that time will show that all the methods adopted by us are extremely valuable in ridding the patient of multiple foci of infection until better methods are devised.

We have come to regard the infection of the teeth as the most constant focus found in our patients. Without exception the functional psychotic patients all have infected teeth. Briefly they may be divided into unerupted and impacted teeth, especially the third molars; periapical granuloma; carious teeth with infection; apparently healthy teeth with periodontitis; devitalized teeth with either Richmond or gold shell crowns; extensively filled teeth with evidence of infection; and gingival granuloma in apparently vital teeth.

While the progressive men and leaders of the dental profession are awake to all these types of infection, unfortunately the "rank and file" are not sufficiently acquainted with these many forms. Consequently the physician who attempts to rid his patient of focal infection must become acquainted with modern dental pathology. In our younger patients, from sixteen to thirty years of age, no matter what the psychosis may be diagnosed, we find unerupted and impacted third molars in a large proportion of the cases. And we would unhesitatingly advise, when there are clinical evidences of systemic infection and intoxication present, that these should be removed. We have found that they are always infected, and the infection is in some way related to the

fact that the tooth is unerupted and impacted. All crowns and fixed bridgework have been condemned by the best men in the dental profession, and we voice the same opinion. So in order to rid a patient of focal infection a very thorough job must be done and no suspicious teeth allowed to remain. This does not mean that every patient should have all his or her teeth extracted. In fact, in our work at the State Hospital we would not average over five extractions per patient.

Time prevents my going into the question of infected teeth more thoroughly, but I would emphasize the fact that a thorough elimination of focal infection can only be obtained by extraction. All other methods have proven worthless and dangerous to the general health of the individual.

We should like to call attention to the method of removing the infected teeth. In many cases simple extraction is not sufficient even when the socket is thorughly curetted. When the alveolar process is severely involved the Novisky method of surgical removal is absolutely necessary. Failures to get results from removing infected teeth are frequently due to the fact that diseased, infected, necrotic bone is left and absorption continues even after the teeth are extracted.

Chronic infection of the tonsils is equally important as infected teeth, and the mouth cannot be considered free from infection when infected tonsils are not removed. It is a striking fact that very rarely is a patient admitted to the State Hospital at Trenton whose tonsils have been previously removed, so that over 90 per cent of the patients have to have their tonsils enucleated after admission. That the children of the present generation are having their infected tonsils enuleated will, we believe, have a definite influence on the elimination of systemic and mental disorders later in life. Whatever may be the result of treating infected tonsils with the roetngen ray or local therapy, we feel that today enucleation is the only method permissible.

Types of Bacteria Concerned in Chronic Infection. Briefly stated, we have found the various types of streptococci and colon bacilli responsible for chronic infection in our psychotic patients. The streptococcus group composes many strains, as cited below. The colon bacillus group is also made of various strains, differentiated by their cultural reactions in carbohydrate media.

Below is given a table showing the strains of streptococci classified according to Holman. These sixteen types represent the grouping of 1122 strains of Holman, and taken with strains from the literature, the total number is 2463, a sufficient number to come to some conclusion as to their biologic types. While some types can be identified under the microscope, only by their cultural reactions can they be accurately differentiated.

HEMOLYTIC STREPTOCOCCI

Type.	Mannite.	Lactose.	Salicin.
Infrequent	Plus	Plus	Plus.
Hemolytic, i	Plus	Plus	Minus.
Pyogenes	Minus	Plus	Plus.
Anginosus	Minus	Plus	Minus.
Hemolytic, ii	Plus	Minus	Plus.
Hemolytic, iii	Plus	Minus	Minus.
Equi	Minus	Minus	Plus.
Subacidus	Minus	Minus	Minus.

NON-HEMOLYTIC STREPTOCOCCI

Fecalis	Plus	Plus	Plus.
Non-hemolytic, i	Plus	Plus	Minus.
Mitis	Minus	Plus	Plus.
Salivarus	Minus	Plus	Minus.
Non-hemolytic, ii	Plus	Minus	Plus.
Non-hemolytic, iii	Plus	Minus	Minus.
Equinus	Minus	Minus	Plus.
Ignavus	Minus	Minus	Minus.

We have so far been able to isolate six strains of the hemolytic group, *i. e.*, the infrequent, pyogenes, anginosus, equi and subacidus, and five strains from the non-hemolytic group, *i. e.*, fecalis, mitis, salivarus, equinus and ignavus. We have found representatives of both these groups in various sources of culture. Occasionally the hemolytic strains are found in the teeth, but more frequently this type is found in the tonsils and gastrointestinal tract. Nine-tenths of the tonsils harbor the hemolytic strains, and often the non-hemolytic strains as well, and it is not unusual to find two or three strains in the culture from the stomach and duodenum, both hemolytic and non-hemolytic types.

Later investigations have shown the "viridans" is a form of the non-hemolytic streptococcus, but not all of the latter can be classed as "viridans." So it is better to substitute the exact type for this term.

It is useless to argue which types may or may not be pathogenic, or which types may be more virulent than others. We have not found that the hemolytic types were more virulent than the other group or that they produced more marked symptoms. In fact, any of these organisms may become so virulent at any time that they cause the death of the patient, although for a long time they may be latent and no marked evidence of their presence shown other than by the fixation tests. We are still of the opinion that the complement-fixation tests of the blood for determining the presence of chronic infections are of value, as are also the agglutination tests for the same purpose. Further standardization is necessary, however, before they can be used as a routine laboratory test.

Dissemination of Infection. From the fact that the elimination of infected teeth and tonsils produced marvellous results in some cases and in others no results whatever, it was logical to conclude that the infection had spread to other parts of the body, through either the lymphatic circulation or the blood stream, and preferably by the former. Secondary infection of the stomach and lower intestinal tract could also come from constantly swallowing the bacteria originating in the mouth, so that we find secondary foci of infection of the stomach, duodenum, small intestine, gall-bladder, appendix and colon. The genito-urinary tract is frequently infected not only by the organism of the streptococcic group but by the colon bacillus group as well. The source of this infection of the genito-urinary tract is not altogether known.

In the females we find at least 80 per cent of the cases have a chronic infection of the cervix uteri, and while the body of the uterus is rarely involved, we more frequently find infection in the adnexia. In the males a certain percentage of the acute psychoses have infection of the seminal vesicles. The prostate and bladder, as a rule, are not involved.

Treatment by Detoxication. It should be evident from what has been said that all surgical measures utilized are primarily for the elimination of the chronically infected tissue. It has no relation to the surgery practised some years ago which was directed toward correcting malpositions and the removal of ovaries and other organs irrespective of infection.

The removal of all infected teeth and infected tonsils is imperative. Surgical measures have been utilized for removing portions or all of the infected colon. The Sturmdorff method of enucleating an infected cervix has proved very successful. When the uterus and adnexa are involved a complete hysterectomy is necessary, and involvement of the seminal vesicles necessitates excision and drainage.

Chronic gastric infection and infection of the small intestinal tract can only be treated by autogenous vaccines or specific serum. Autogenous vaccines are made in our laboratory from the bacteria isolated from the stomach by the Rehfuss method. We have also developed a specific antistreptococci and anticolon bacilli serum made from the organisms isolated in our laboratory. Every patient receives as routine treatment, first, the autogenous vaccine and later the specific serum. But always after infected teeth and tonsils have been removed. The serum has proved especially valuable in the operative cases. Its administration before operation upon the colon has reduced the mortality from 30 to 12 per cent. Therefore if for no other reason its use is justified.

I shall leave to others a detailed discussion of the gastrointestinal infection and the infection of the genito-urinary tract.

Results of the Work. We have outlined above our theories regarding the causation of the so-called functional psychoses. We realize that many theories have been advanced in the last fifty years regarding this subject, but we also want to state that during this time the recovery rate of state institutions has materially diminished. If then we advanced merely a new theory and could not show that the application of such a theory had had unusual results on our patients, we should then be classed with the theorists and our work considered interesting if true. However, we feel that we have substantial grounds for considering that the application of these theories has produced results which, as Meyer states, "Appear to have brought out palpable results not attained by any previous or contemporary attack on the grave problem of mental disorder."

We will confine our statistics to the so-called functional group, which includes dementia precox, manic-depressive insanity, paranoid conditions and the psychoneuroses. In this group, as a whole, for a ten-year period prior to 1918 the recovery rate was only 37 per cent of the admissions. Since 1918 the recovery rate has averaged nearly 70 per cent in the same group. Of 380 cases classified in this group in 1918 only 50 today remain in the hospital, and 9 of these are criminals. A recent survey made of these 380 patients discharged in 1918 shows that after three years, with few exceptions, they are today normal in every respect. Over 1000 patients have been successfully treated in the last three years, and it is gratifying to note that the proportion of readmissions to the State Hospital at Trenton has not increased during this time, and that many of the readmissions are cases that were admitted, the first time, prior to this period of intensive treatment.[1]

Our failures have been confined to the patients with a psychoses of over two years' duration. The cause for such failures we consider is due to the fact that the brain has become permanently damaged and no amount of elimination of such infection has any effect upon the psychosis.

Conclusions. We have produced evidence, both clinical and pathologic, which should set at rest any doubt as to the accuracy of our deductions. The fact that many individuals harbor focal infections and are not insane is no argument against the doctrine that focal infections can cause insanity. We know that only a small proportion of patients contracting syphilis develop paresis. In the same way we know that only a small proportion of those indulging in alcohol excessively develop a psychosis. Some individuals are able to drink a great deal without showing any symptoms, and in other individuals it takes only a small amount to produce a psychosis.

[1] On July 1, 1922, the successfully treated cases numbered 1400, and only 50 (or 3 per cent) have returned and are still in the hospital.

One may argue similarly regarding a functional psychosis. The type, specificity and severity of the infection, plus the patient's constitutional lack of resistance, determine whether or not a psychosis will develop. Such factors as heredity and psychogeneses undoubtedly play an important role; more, however, we now think, as precipitating the psychosis rather than as causing it.

THE APPLICATION TO OTHER INSTITUTIONS OF THE RESULTS OF TREATMENT OF THE INSANE IN TRENTON STATE HOSPITAL.

By Burdette G. Lewis,

STATE COMMISSIONER OF INSTITUTIONS AND AGENCIES OF NEW JERSEY.

It is naturally very gratifying to me to note the success in New Jersey of work which I undertook in New York, but which for want of time I was never able to carry through to completion. While Commissioner of Correction in the City of New York, I undertook to transplant to the old correctional institutions of the city and to the two new reformatories many of the routines and practices of the best hospitals for the insane. We discovered that many men and women in prison or in the reformatory were either insane or unstable, or were epileptics or feeble-minded, or were not able properly to conduct themselves as normal beings. We also discovered that the disciplinary difficulties of correctional institutions were almost entirely due to the presence of persons belonging to these various groups who had been sentenced to prison or to a reformatory. By inquiry among the best hospitals for the insane and the best institutions for the treatment of the unstable, the epileptic and the feeble-minded, we found that the disciplinary difficulties of such institutions had been solved not by the club and the gun and by invoking horrible imprecations and profanity, but by the intelligent application of modern therapy and modern treatment, with which physicians have now become quite familiar.

The organization of the New Jersey Department is such that work which was difficult in New York, where the departments were under separate jurisdiction, is very simple in New Jersey, where all of the institutions are in a single department. This has made the transplantation of the best practices of the particular institution to all the other institutions a much simpler problem. Take, for example, mental and medical work in the correctional institutions. Here we organized a psychiatric clinic and placed the doctors and the psychologists under the general supervision of Dr. Cotton, who holds the position not only of Medical Director

of the State Hospital at Trenton but also of Acting Director of the Division of Medicine and Psychiatry of the Central Department. This plan has hastened the application of the best tested results of the State Hospital to all the correctional institutions. Cases are discovered in the correctional institutions which are in need of treatment at the hospital, and under our law they are transferred to the psychopathic division of the hospital long before they have become insane from the legal viewpoint.

The influence of the psychiatric clinic upon medical work of the institutions has been very great. The treatment of the mouth, the removal of tonsils, the clearing up of gastrointestinal infection, the development of surgical procedures and the all-around treatment of the individual which is carried out at the Trenton Hospital have shown the desirability of extending the benefits of such medical, surgical, and other treatment to all of the population of each correctional institution. In consequence the medical service and the appropriations for medical service have been more than trebled in all the institutions. The expense of this has been reduced by reason of the fact that the psychiatric clinic cuts down the cost of overhead supervision of physicians and by reason of the fact that the increase in the amount of medical work in each institution has stimulated coöperation with the physicians of the various communities in which the various institutions are situated. The amount of voluntary work performed by physicians in connection with our institutions has been more than quadrupled in the last three years. It is obvious, therefore, that we are deeply indebted to the physicians in regular practice throughout the state for many of our good results. We found, for example, at the State Home for Boys, an institution for juvenile offenders, that at least 65 per cent of the boys were in need of minor operations; that only 3 per cent of them had the benefit of such operations before reaching the institution. A group of twenty physicians has voluntered to help in the work which has been going forward in that institution for more than a year. We have also changed the personnel and improved the scholastic and other work which is carried on for these boys. The results speak for themselves. Three and a half years ago one out of each two boys released from that institution upon parole failed, now only one out of each ten fails.

The development of research work at Trenton has stimulated similar work in other institutions, and has won for us legislative appropriations for treatment instead of mere custody of patients. Morris Plains State Hospital, for example, has under the course of construction a 400-bed treatment hospital, which will permit the carrying out of the very best types of medical treatment at that institution. Our plans call for the provision of additional buildings at the Morris Plains Hospital and at the Trenton Hospital,

so that each institution will in fact be two institutions, one for the medical treatment of new cases and of the cases which have been in the institution for only a short time, and the other institution for the chronic cases which are beyond reasonable hope of recovery.

We are attempting to extend to the people of our various communities the results of these achievements in the institutions through the establishment of clinics. There is not time to go into details, but suffice it to say that the physicians in our state institutions are to secure the advantage of handling the new cases in the communities long before they would ever reach a state hospital. On the other hand, the patients in the state institutions are to reap the benefit of the enthusiasm of doctors whose efforts are stimulated by contact with mental disease in the earlier stages of its develment; for you physicians, I am sure, fully realize how, perhaps unconsciously, hospital physicians fall into the rut and feel that there is little use of extensive work upon cases which have become chronic in so many instances before they reach the state hospital.

We are deeply indebted to men like Dr. John W. Draper, who has so freely given up his time and his expert abilities in the promotion of our work, at no small sacrifice of time and strength. New Jersey is indeed fortunate in securing their help, and is proud of the results achieved.

CARCINOMA OF THE ESOPHAGUS WITH PERFORATION OF THE AORTA: OBSERVATIONS ON RADIUM THERAPY.

By James G. Carr, M.D.,

and

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Chicago.

Perforation of the aorta complicating carcinoma of the esophagus is of infrequent occurrence. There is a curious similarity in most of the statistical reports regarding the relative frequency of such perforations. Hampeln[1] found 2 cases of perforation in the aorta in 57 autopsies on subjects dead of esophageal carcinoma. Mampell[2] saw two such perforations in a series of 50 autopsies. Taylor[3] quotes Ewald thus: "In 40 to 50 cases of carcinoma of the esophagus I have only known 1 to perforate the aorta." Knöpfler[4] refers to Eichhorst's series in which perforation of the aorta was found once in 34 cases, and also quotes Petri's statistics of 44 cases, with 1 instance of aortic perforation and 2 of perforations of intercostal arteries. Very different figures were given by

[1] St. Petersburg med. Wchnschr., 1903, **20**, 423.
[2] Inaug. Diss., Ueber den Speisenrohrkrebs, 1904.
[3] Lancet, 1896, **1**, 991.
[4] Inaug. Diss., Zur Casuistik des Ösophagus Carcinoms, 1900.

v. Ziemssen and v. Zenker as quoted by Hess[5] and Knöpfler.[4] This analysis of 116 cases included 18 of perforation of the aorta.

In 1896 Knaut[6] collected all the reported cases of perforation of the aorta as a complication of carcinoma of the esophagus. The first case he found was reported by van Doevereen in 1789. Knaut's review of the cases in the literature included perforations of other large vessels. He believed such perforations to be very rare and quoted Leichtenstern to this effect: "Perforations of the aorta and vena cava are most rare." Taylor collected 8 cases in 1889 and in 1895 Vierhuff[7] cited 8 cases with this remark: "The cited 8 cases of perforation of an esophageal carcinoma into the aorta are the only ones found in the literature." Neither Taylor nor Vierhuff could have known of the statistics of v. Ziemssen and v. Zenker.

Knaut's series included 50 cases. Among these there were 32 of perforation of the thoracic aorta and 2 of the aortic arch. Twice the left common carotid was perforated; twice the left subclavian. The left internal carotid, the right subclavian and the esophageal artery were each perforated once. In 1 case the first, second and fourth intercostal arteries were involved; in another the esophageal vein was perforated; while the portal vein was opened once by a growth originating in the lower part of the esophagus. In 2 cases mention was made of "aortic branches" as the source of the terminal hemorrhages without further details, while the source of the hemorrhage was undetermined in 1 other case; here there remained a question as to whether the left common carotid artery or the left jugular vein was ruptured.

The series included 3 cases in which no actual perforation had occurred. In 2 of these the wall of the left auricle showed carcinomatous invasion; in 1 of these cases a cerebral embolus was the cause of death; in the other the statement was made that there were cerebral symptoms late in the course of the disease. In the third case there was a thrombus beginning in the right azygos vein, extending into the superior vena cava and thence to the right auricle.

Since Knaut's publication we have found 21 cases in the literature, including, as Knaut did, perforations of the aorta and large vessels. The first case reported subsequent to Knaut's paper was that of Taylor;[8] there was a perforation of the descending aorta about two and one-fourth inches below its commencement. Drozdowski,[9] Garrod[10] and Mader[11] each reported cases of "per-

[5] Inaug. Diss., Ueber Perforationen bei Oesophaguscarcinom, 1902.
[6] Inaug. Diss., Berlin, 1896.
[7] St. Petersburg med. Wchnschr., 1896, N. F., **13**, 195.
[8] Loc. cit.
[9] Russk. Arch. patol. klin. Med. u. Bakteriolog., 1896, **1**, 557 (quoted by title).
[10] Tr. Path. Soc. ,London, 1897–8, **49**, 92.
[11] Jahrb. Wien. K. K. Krankenanstalten, 1897, **6**, Pt. 2–207.

foration of the aorta." Moore's[12] case was diagnosed clinically as aneurysm: "The absence of anything resembling cancerous cachexia or of any constitutional disturbance and the presence of a whole group of pressure symptoms led me to the belief that the lesion was most likely an aneurysm." Sudden death followed a profuse hemorrhage; at autospy there was found a perforation of the right subclavian artery. Finley and Anderson[13] reported a case of perforation of the left subclavian artery. Yepifanoff's[14] case was one of perforation of the right common carotid. In Mauclaire's[15] case a perforation of the transverse portion of the aortic arch occurred some six months after a successful gastrostomy. Knöpfler's[16] case was one of perforation of the aorta about the level of the bifurcation of the trachea. Minnich[17] merely reported a case of perforation of the aorta without further specifications. The case of Biggs[18] was like that of Mauclaire; three months after a successful gastrostomy the perforation occurred. The cases of Hollos[19] and of Hart[20] were perforations of aortic aneurysms. Hampeln[21] reviewed his autopsy records of 57 cases of esophageal carcinoma; the series included 2 cases of perforation of the aorta; anatomic details were not discussed. In Davidsohn's[22] case there was a very small communication between the aorta and the esophagus; the stomach contained a quart or more of blood. Mampell[23] analyzed the autopsy records of 50 cases of esophageal carcinoma; perforation of the aorta was recorded once; there was a further record of perforation of an intercostal artery. In Guy's Hospital Reports[24] for 1905 there is a record headed: "The aorta opened by an epithelioma of the esophagus." Deve's[25] case was one of latent carcinoma of the esophagus, which terminated very suddenly; at autospy a perforation of the thoracic aorta was found. Levy, Valenski and Godlewski[26] reported another latent case, "Clinically without symptoms of esophageal disease" a "foudroyante" hemorrhage occurred; autopsy disclosed a rupture of the aorta in association with ulcerating carcinoma of the esophagus. In addition to these cases of actual perforation Hess[27] described an extension of the carcinomatous process to the wall of the left auricle; "The wall is permeated by firm, whitish tumor masses, which are connected with the tumor masses originating in the esophagus."

[12] Dublin Jour. Med. Sci., 1898, **105,** 396.
[13] Montreal Med. Jour., 1899, **28,** 125.
[14] Bolnitsch. gaz. Botkina, St. Petersburg, 1901, **12,** 522 (quoted by title).
[15] Bull. et mém. Soc. anat. de Paris, 1901, 6 S, **3,** 256.
[16] Loc. cit.
[17] Pest. méd. chir. Presse, 1902, **38,** 941. (quoted by title).
[18] Proc. New York Path. Soc., 1903–4, **3,** 1.
[19] Pest. Med. Chir. Presse, 1903, **39,** 357 (quoted by title).
[20] Zeitsch. f. Krebsforschung, 1905, **3,** 278.
[21] Loc. cit.
[22] Deutsch. med. Wchnschr., 1904, **30,** 409.
[23] Loc. cit.
[24] Guy's Hosp. Reports, London, 1905, **19,** 396.
[25] Revue méd. de Normandie, 1907, **8,** 95.
[26] Bull. et mém. de Soc. anat. de Paris, 1910, **35,** 140.
[27] Loc. cit.

Vierhuff[28] and Hart[29] discussed the pathogenesis of such perforations. Vierhuff expressed the opinion that the wall must be diseased before the perforation occurs; "The wall of the aorta must undergo carcinomatous degeneration to supply the conditions for perforation." Hart saw "the occasion for the perforation in the advance of gangrenous destructive processes." Opinions such as these have found general acceptance.

The case which we report was seen at the County Hospital on the service of Dr. Joseph A. Capps, through whose courtesy the records have been placed at our disposal.

S. S., aged forty-five years, male, in preprohibition days a bartender by occupation, was admitted to the hospital on June 3, 1920. He complained of loss of weight, pain in the chest, difficulty in swallowing and regurgitation of food. The difficulty in swallowing had been present for three months; at first only solid foods, especially large particles of the same, caused the dysphagia, but the condition was aggravated until upon admission it was possible for him to swallow only liquid or soft foods; the act of swallowing such foods was associated with sharp, shooting pain in the chest. There was some thoracic pain most of the time. This pain was localized particularly about the midsternal region. Unless the food was taken very slowly regurgitation occurred. Aside from a history of alcoholism, including an attack of delirium tremens sixteen years previously, his personal and family history was negative. Physical examination was generally negative. The Wassermann reaction was negative. Roentgen-ray examination on June 4, disclosed: "A partial obstruction in the middle third of the esophagus. This narrowing is irregular in character and indicates an extensive lesion, probably malignant."

Beginning June 21, radium therapy was employed with fluoroscopic control; "The end of the metal container is seen to lie in the substance of the growth as evidenced by the barium shadow at the site of the lesion." Further treatment was given on June 22 and 24 and on July 26. On August 24 examination (roentgenologic) showed "considerable deformity of the esophageal walls, although very much less so than on previous examinations." There had been distinct clinical improvement; semisolid food was taken easily; the weight and strength had increased. At his own request the patient left the hospital September 21; prior to his discharge he had been taking general ward diet. Arrangements were made to continue the radium therapy.

Treatments were given October 16 and 23. On October 16 a note was made: "The shadow of the radium tube is seen to lie

[28] Loc. cit. [29] Loc. cit.

in the area of the lesion." On December 2 he returned for another exposure. The roentgenologist reported: "There is seen an obstructive lesion in the middle third of the esophagus which supports the previous roentgen-ray finding of carcinoma. This examination seems to indicate an improvement of the lesion, as the barium passed through the obstruction with much greater ease than previously noted."

He was again admitted to the hospital on December 21. Two treatments were given, December 22, 1920, and January 13, 1921. On January 21 the esophagus was dilated with a No. 29 dilator: Tight, but bulb passed without much force. Five days later, about 9.30 P.M., the patient complained of a marked burning in the abdomen shortly after taking some veronal. Pallor and weakness of the pulse came on rapidly. Death occurred at 11.50 P.M. Shortly before he expired he coughed up some bright red blood.

Autopsy, performed on the following morning, revealed a carcinoma of the esophagus, about the level of the hilum of the lung: "There is a hard mass, 6 to 8 cm. in length, about the region of the hilum of the lung. This mass encircles the esophagus." The inner surface of the esophagus showed an ulcerating area over approximately the lower half of the mass described. The upper half of the mass was hard, fibrous, with a rough inner surface without ulceration; there appeared to be well-marked fibrosis, indicating a healing process. Within the ulcerated area described there were two small perforations connecting the esophagus with the aorta. A large quantity of blood was found in the stomach.

The perforation of the aorta, rare as it is, is not the only feature of unusual interest in this case; from the practical standpoint the bearing of the autopsy findings upon the efficacy and the difficulty of successful radium therapy is even of more interest.

Radium therapy of esophageal malignancies has to contend with certain problems as yet unsolved. The disease is insidious in nature and has often invaded neighboring organs before the symptoms have become sufficiently disturbing to send a patient to the physician. Carcinoma of the esophagus spreads by continuity of tissue; far less often do metastases occur. In the patient apparently improving, with less obstruction, greater ease of swallowing, some gain in weight and strength, symptoms of pulmonary involvement often supervene or other symptoms appear, such as pain from pressure or respiratory obstruction, due to the presence of a secondary mediastinal tumor. To these causes of failure must be added the technical difficulties of the introduction and location of the radium; the diseased area must be sufficiently dilated to admit the capsule containing radium; emplacement must be controlled by fluoroscopy. It appears from the autopsy cited that one portion of an esophageal carcinoma may be treated

successfully while another portion is missed altogether. Certainly such an interpretation may be placed on these findings, though it must be admitted that the varying effect of radium might cause an irritative effect in one area, a healing one in another. Yet it seems justifiable to emphasize the former view, to point out that evidence of healing has been demonstrated in an esophageal carcinoma hand-in-hand with an actively progressive process. Fluoroscopic control does not necessarily mean treatment of the entire tumor. Under fluoroscopic control accurate measurements must be made as to the location of the tumor and its length. Finally it is not enough to insert the radium from above. Until the tumor, for its entire length, is permeable to a sufficient degree to admit the capsule, so that the capsule may be passed the entire length and redrawn into the area, to be located at different levels, we cannot feel that our technic is directed to the treatment of the accessible growth in its entirety.

Summary. 1. Since the publication of Knaut, in 1896, 21 cases of esophageal carcinoma with perforation of the aorta or other large vessels have been reported. Another case is added here.

2. Autopsy findings in the case here reported disclosed certain deficiencies in the application of radium therapy. Suggestions are made for more effective technic.

NOTES ON STUDIES IN THE PHYSIOLOGY OF THE GALL-BLADDER.*

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An increasing interest has been shown by the medical profession in various types of non-surgical biliary drainage; the reaction of the gall-bladder and its associated structures to the application of supposed biochemical and physiologic agents has been utilized in the diagnosis and treatment of disease of this organ.

Last year we began a series of studies, anatomic and physiologic, into the nature of certain biliary phenomena alleged to occur as a result of treatment of the duodenal mucosa and the papilla

* These experiments were performed in the Laboratory of Physiology of Cornell University Medical College. We wish to thank Dr. Graham Lusk for his kind interest and encouragement and for his courtesy in extending to us the facilities of the laboratory.

of Vater by magnesium sulphate and other agents. As a result of these studies we present the reports of a series of animal experiments upon the action of magnesium sulphate when applied to the duodenal mucosa and the papilla of Vater, the rate and character of resultant bile flow, the contraction of the gall-bladder and the question of stasis of bile in that organ.

I. Anatomy of the Bile Passages. The gall-bladder[1] is a small pyriform sac, lying obliquely on the inferior surface of the liver; it is considered generally as an embryonic diverticulum of the hepatic duct, enlarged at its extremity to act as a reservoir for bile. Its duct, the cystic duct, joins the hepatic duct to form the ductus choledochus or common bile duct; it meets the pancreatic duct at the papilla of Vater and there empties into the second part of the duodenum. The position of the organ is such that on account of the double mesial curve of the neck and the attachment of the body the fundus is lower than the point of exit of the duct into the duodenum, necessitating an upward flow of its contents if they are to be expelled.

The wall of the gall-bladder is composed of three coats: An outer coat of peritoneum, a middle coat of smooth muscle and fibrous tissue and an inner coat of mucous membrane which presents a reticulated appearance due to the plicæ or ridges into which it is thrown. There are also a number of mucous glands of fairly large size described by Luschka,[2] who found from three to twenty of these glands in the gall-bladder. They are lined by long cylindrical cells giving the appearance of being ciliated cells. Holmes[3] describes a series of mucous glands scattered throughout the whole mucosa of the bladder and ducts.

The muscular coat is one of more than ordinary interest in connection with the function of the organ. Sparsely distributed unstriped muscle fibers are interlaced with fibrous tissue in this layer; most of the muscle bundles run longitudinally, a few transversely. These fibers are irregularly continued in the corresponding coat of the duct and at times seem to be thickened in an attempt at sphincter formation; this is especially noticeable near the junction of the cystic and hepatic ducts, as first described by Tobien.

At the opening into the duodenum, however, the papilla of Vater is found. This structure is of peculiar interest to us from an anatomic and physiologic standpoint on account of its known definite sphincteric function and its part in the control of bile flow. Our first real knowledge concerning the existence of a definite muscular mechanism at this point we owe to Oddi,[4] who described what he thought to be an individual set of muscular fibers surrounding the terminal portion of the common bile and pancreatic ducts. While earlier anatomists indicated the existence of such a mechanism the maceration experiments of Oddi on the

terminal ducts and papillæ of animals demonstrated existence of a set of circular muscle fibers which have since been named after him. The fibers had their origin in the circular fibers of the duct. As the duct entered and traversed the wall of the intestine the bundles were seen to thicken and lengthen, throwing out lateral fibers which mingled with the longitudinal and circular fibers of the intestinal wall, thus apparently forming "points of support" for the duct in its course. The resulting sphincter-like formation was declared by Oddi[5] to be separate and distinct from the intestinal musculature. This structure was seen to be especially developed in the sheep, dog, ox and pig. He showed, moreover, that the tone of the sphincter was such that it had a resistance of 50 mm. Hg (675 mm. water), which exceeds the normal secretory pressure of bile by 475 mm. of water.

Hendricksen[6] in his observations upon the dog, cat, rabbit, and guinea-pig confirmed the findings of Oddi and was furthermore able to demonstrate the existence of an anatomical sphincter of similar nature in man.

We have been able to demonstrate without difficulty the existence, in dogs and in man, of circular bands of smooth muscle fibers surrounding the common bile duct in its course through the intestinal wall. By the study of microscopic sections these transversely arranged bundles are seen to be continuations of the previously described scanty musculature of the gall-bladder and the first and second portions of the common duct. In the third portion, such as described by Oddi and Hendricksen, they were seen to lengthen and thicken and become more numerous, but at no point do we see the formation of a compact distinct muscular bundle conforming to our conception of a true sphincter such as, for example, the sphincter of the pylorus, the compressor urethræ, the sphincter ani, etc.

Our observations upon the microscopic sections prepared from three dogs and three human specimens indicate that the muscular fibers of the sphincter are scanty, widely separated and diffuse and are at no time continuous. It is our impression that there is a fusion of the fibers of the intestinal muscularis with the corresponding layer of the duct which goes to make up the muscular apparatus of the papilla. That there is, however, distinct sphincteric action will be shown in a later discussion of the mechanism and function of the papilla.

The anatomic structure of the gall-bladders of dogs and man are similar.

That the gall-bladder is not essential to the well-being of the individual is seen from the normal lives led by persons after complete cholecystectomy. Likewise there are no ill effects noted in cases of congenital deformities of the gall-bladder, in which there may be partial septa or other changes. The presence of

two distinct gall-bladders has been recorded, and Gay[7] writes of 19 cases of complete absence of the gall-bladder in man. Schachner also cites 7 cases of congenital absence of the gall-bladder. Wilder[8] in discussing the slight physiologic importance of this organ and its lack of universal occurrence gives the instance of its presence in one of two animals of the same family—the fowl, whereas the pigeon has none. The gall-bladder likewise is lacking in the horse, mule, ass and elephant. (Rolleston[9].)

Oddi and others, particularly Rost,[39] however, speak of a "compensatory" dilatation of the ducts following cholecystectomy.

With the exception of Gray,[1] who states that the gall-bladder is innervated by a branch from the celiac plexus, the writers of text-books of anatomy are rather vague concerning the nerve supply of the organ. A great amount of work has been done in this field, however, the outstanding feature of which is a disagreement as to the specific nature of the impulses passing to the organ.

Perhaps the earliest report on the subject is given by Oddi,[10] who claims for the sphincter special spinal-cord ganglion centers which regulate its tone. The location of this center he places, in dogs, at the level of the first lumbar segment. The mechanism he regards as an inhibitory reflex. Meltzer[42] in his studies upon contrary innervation and inhibition comments on a system of crossed innervation for the gall-bladder and sphincter, a system which would cause a contraction of the gall-bladder simultaneous with a dilatation of the sphincter, and *vice versa*. The application of the law of contrary innervation calls for a double innervation, splanchnic and parasympathetic, to the bladder and papillary muscle. It is presumed that the vagus contains motor fibers for the sphincter and inhibitory fibers for the gall-bladder. During digestion the pair of fibers in the splanchnic are brought into play and are supposed to cause the expulsion of the bile from the gall-bladder. Thus the same stimulus that traversed the splanchnic system to cause contraction of the gall-bladder would simultaneously relax the sphincter; or, travelling through the vagus system, would contract the sphincter and relax the gall-bladder.

Physiologists are not convinced about the experimental data upon which this theory rests. Doyon[11] in extensive experiments on stimulation of the peripheral end of the splanchnics found contraction of the gall-bladder and the bile ducts.

The contraction of the ducts, moreover, may produce complete obliteration at least at one point. On stimulation of the central end of the splanchnics he found relaxation of the sphincter. Doyon says that he never saw these two results produced simultaneously but presumes that they occur. Excitation of the peripheral end of the vagus was usually without effect. In one dog the author noted a contraction of the sphincter.

Bainbridge and Dale,[12] on the other hand, covering the same ground more than eleven years later, came to conclusions diametrically opposed to those just cited. Following the Doyon technic they noted upon section of both vagi and splanchnics an increase of pressure transmitted by the balloon in the gall-blader (from 15 cm. of water to 50 cm.). They found that the "invariable result of faradizing the splanchnic nerve was relaxation of the gall-bladder." Stimulation of the cut end of the vagus in the thorax gave rise to contraction of the gall-bladder. By means of a balloon in the gall-bladder, rhythm and tonus were demonstrated by all the foregoing authors. Contractions of the gall-bladder were evidenced by rise of manometric readings in an instrument connected with the balloon. Okada[13] also reports rhythmic contractions of the organ. A clear-cut demonstration of the law of crossed innervation, so far as its application to the gall-bladder is concerned, has, however, not yet been seen.

Physiology of the Gall-bladder. That the gall-bladder is a functioning organ which operates in a definite and characteristic manner has been upheld by physiologists generally for many years. The unanimity of opinion held by the writers[14] of standard text-books and reference-books is so striking as to suggest the complete absence of any attempt on the part of these authors to verify by actual observation the description of the mechanism as handed down from one author to the other.

The gall-bladder is held by all to be a reservoir for the storage of bile which is continuously secreted by the liver; such secretion is kept for intermittent periodic discharge into the intestine only during the active digesting period of the individual's day. According to the present conception, in the fasting state, bile passes down the hepatic duct and is shunted off into the gall-bladder, where it remains. Upon the passage of acid chyme from the stomach into the duodenum a reflex mechanism is excited whereby the papilla of Vater is relaxed, the wall of the gall-bladder contracts and the bile stored there is ejected into the duodenum along with an increased flow of liver bile.

Mann[15] emphasizes two other functional possibilities of the gall-bladder—secretion and the regulation of flow, in addition to the reservoir action.

That there is a definite tone to the sphincter and to the gall-bladder itself has been shown by many observers. Freese,[16] Judd and Mann,[17] Okada[18] and others hold a brief for the contractility of the organ and the sphincter, but that this contractile power is small and weak is generally agreed. As a matter of fact the musculature of the wall is so sparse that we found it impossible in dogs to obtain by strong direct faradic stimulation even the slightest contraction visible to the eye or sufficient to expel any

of the contents.* The effect of drugs on the contractility and tonicity of the isolated gall-bladder has, however, been worked out by Lieb and McWhorter.[19] These authors found an increase in tonus due to myoneural parasympathetic stimulation with pilocarpin and physostigmin and a relaxation with atropin and adrenalin. Other drugs, too, showed varying effects.

The secretion and excretion of bile is a subject which is dismissed in all too cursory a manner by most text-books. Although some authors declare that the carbohydrate fraction of a meal has but little if any effect upon bile flow, they place great emphasis upon the activating property of the acid chyme of the stomach, in some cases regardless of its constituents. The stimulation of bile expulsion given by dilute HCl was shown in 1880 by Rutherford.[20] Okada[21] bears this out by his experiments with hydrochloric acid, in which he induced a bile flow by its application. He further studied the effects of cholagogues, noting marked positive effects with peptone, bile, bile salts, sodium salicylate, chloral, salol, pilocarpin and nicotin.

Voit[46] first noted the variations in bile flow during digestive processes. Perhaps the best study of the effect of foodstuffs, however, is that of Bruno,[22] who determined that not all foodstuffs are active in stimulating bile flow. As a result of a series of painstakingly detailed experiments with a Pawlow fistula in dogs he concludes that there is no psychic secretion of bile. The flow ceases as soon as the stomach is empty. The arrival of bile in the intestine is determined by the digestion of food in the stomach. The progress of the excretion of bile is more or less typical for the type of nourishment taken. The reaction of the duodenal contents, moreover, does not play the role of exciting this secretion. Water by itself did not excite the bile flow nor did albumin alone. The arrival of bile in the intestine, Bruno says, is dependent upon the chemical action of the products of digestion of albuminous bodies. Starch is not an excitant, but if meat powder is added a flow is obtained. Fats show a marked positive action. Extractives such as Liebig's meat extract show a specific action.

Bayliss and Starling[23] have shown that secretin acts upon the liver in a manner similar to that by which it induces the flow of pancreatic secretion. The contact of the HCl with the duodenal mucosa activates a hormonic substance, secretin; they noted the absorption of this product into the blood stream and the subsequent effect of secretory stimulation of the liver cells by the secretin.

Fleig[24] observed an acceleration of bile flow in chloralized dogs after the introduction of oil into the duodenum.

If the gall-bladder is to act as a reservoir or flow regulator for

* The strength of current used (six dry cells with an inductorium) was sufficient to cause, when applied to any part of the stomach or to the small or large intestine, a distinct segmental tonic spasm.

bile in transit its contents should not vary materially in composition from the material excreted directly from the liver. Moreover, to fulfil one of the functions attributed to it, that of secretion, it must have a secretory mechanism. That it has a secretory, and possibly an absorbing, function is undoubted, but not for the secretion of bile. Anatomically the only secreting tissue seen in the wall of the bladder are the mucous glands of Luschka, mentioned above. These glands, and the lining epithelium, may, however, have some excretory function, such, for example, as the excretion of toxic substances and chemicals. F. C. Mann's[25] work in the production of chemical cholecystitis practically specific after the intravenous injection of Dakin's solution is interesting in this regard. Of great interest are the differences in composition of the "liver bile" and the "gall-bladder bile."

Hammarsten,[26] Rosenbloom,[27] Hoppe-Seyler and Yeo and Herroun have investigated the quantitative relationships of the constituents of bladder bile and bile from a biliary fistula. The demonstrations are definite in their evidence concerning the greater concentration of the bladder bile over the so-called liver bile, Hammarsten giving the total solids in bladder bile as about eight times that of liver bile. During its stay in the gall-bladder the bile loses a large amount of water and has added to it mucin and albuminous material. Rous and McMaster[28] in a recent study have also given attention to the differences in quality of these two varieties of bile. They further showed that the inspissation of bile in the gall-bladder may proceed with great rapidity. This has its bearing upon the concentration of cholesterol and the subsequent formation of gall-stones. For the latter, however, there must be long-continued stasis, which, if the claims for the functions of the gall-bladder are true, is normally well-nigh impossible in an actively eating and digesting individual.[29]

Hawk[30] puts the amount of normal bile secreted by an adult man during twenty-four hours at from 500 to 1100 cc according to various estimates. Comparing this relatively large output with the normal 30 cc capacity of the gall-bladder, Mann suggested that in no animal could the gall-bladder contain more than 5 per cent of the bile secreted in twenty-four hours, and in most cases only 1 per cent. The plausability of this remark becomes thus apparent.

Clinical Aspects. About four years ago Meltzer[31] published an article in which he discussed the basis of our conceptions regarding the innervation of the gall-bladder and its contractile mechanism. In this article he dilated upon the function of the sphincter at the ampulla of Vater and the interrelation between the contracting gall-bladder and the sphincteric action, as has been described earlier in this paper. Applying the facts made known about the "law of contrary innervation," he invoked this

principle to explain the physiologic coördination of contracting musculature and relaxing sphincter. Meltzer took a step forward and suggested that occasional types of jaundice, such as catarrhal and emotional jaundice, could be caused by disturbances in the carrying out of these coördinated nervous reflexes. He suggested an abnormal rigidity or passivity as the possible cause. He made the practical therapeutic suggestion that a concentrated solution of magnesium sulphate introduced into the duodenum through a duodenal tube might by causing a relaxation of a badly functioning sphincter at the papilla tend to relieve the jaundice.

Lyon,[32] in adopting the suggestion of Meltzer, carried the argument a step further. If magnesium sulphate relaxes the sphincter, then by the law of contrary innervation causes simultaneous contraction of the gall-bladder with the consequent expulsion of its contents. By collecting the fluid in the duodenum after such a saline lavage he proposed a diagnostic test for disease of the gall-bladder based on a study of the amount, character, cytology and bacteriology of these contents under normal and abnormal conditions. He has reported also a characteristic return of differently colored specimens of bile after magnesium sulphate lavage. By means of these color differences he claimed to be able to designate the various parts of the gall tract from which the bile flowed in succession—duct, gall-bladder, hepatic ductules.

That the publications of Lyon have aroused a good deal of speculation and interest in the medical profession is evidenced by the accumulation of a large amount of literature on the subject in the past three years. There have been many papers confirming in effect the claims of Lyon. On the other hand, Einhorn,[44] Reiss, Crohn, and Radin[45] and others have presented evidence against accepting the idea that the dark "B" bile extracted from the duodenum after magnesium sulphate lavage comes from the gall-bladder. At this writing, moreover, there appears the report of the striking observations of Dunn and Connell,[35] who, experimenting with a duodenal fistula in a person after cholecystectomy, obtained the same results as described by Lyon, albeit the gall-bladder had been removed. The stimulation of flow was seen even after the application of the solution at a point distant from the papilla (rectum) and likewise after the passage of the magnesium sulphate through the stomach.

II. Experimental Studies. In the following experiments normal dogs were used, some in the fasting and some in the digesting state, as indicated under such experiment.

Anesthesia. The animals were anesthetized with a solution of chloretone in Mazola oil injected intraperitoneally, the dose being gauged to give complete surgical anesthesia according to the weight of the animal. We chose chloretone rather than ether, chloroform or morphin on account of its easy handling, its lack

of side action and excitement stage, and, as far as we could determine, the absence of any pharmacologic or physiologic action of the drug which might in any way invalidate the observations on the gastrointestinal system.

Operations. All operations were carried on in a warm room with due precautions against interference with normal function on account of shock or trauma. All exposed portions of the animal during laparotomy were covered with cloths wet with warm physiologic saline solution. In cases requiring duodenotomy, periods of from fifteen minutes to half an hour were allowed before manipulations and observations were made; this was done in order to eliminate any inhibitions due to trauma occasioned by incisions.

1. *Action of Magnesium Sulphate.* A series of eight dogs were experimented with in order to test out the "specific" action of magnesium sulphate when applied to the duodenal mucosa in the region of the papilla of Vater. Laparotomy was performed and 2 to 5 cc of a solution of methylene blue in 0.9 per cent saline solution were injected into the gall-bladder of the animal in order to differentiate between bladder bile and liver bile. Three of the dogs in this series were used after fasts of over twenty-four hours. The others were fed either before the start of the experiment or an hour previously.

Observation of the gall-bladder immediately after laparotomy and before injection showed moderately distended gall-bladders in all of the dogs except one which showed a flaccid bladder. The flaccid non-distended bladder was seen in a fasting dog.

After a fifteen minute wait the duodenum was incised at the site of the opening of the bile duct. In all but two animals, one fasting and one digesting, there was noted a slow flow of bile soon after opening the duodenum. This was also true of the two other fasting dogs of the series which showed a fairly continuous, though scanty bile flow from the papilla.

In no case was there any evidence of the methylene blue in the intestine. After a wait of from fifteen to thirty minutes the site of the papilla was gently irrigated with a warm 25 per cent solution of magnesium sulphate in water. The gall-bladder and papilla were closely observed during intermittent irrigations made over periods averaging three hours for each animal. Between irrigations the duodenal area was washed with normal saline solution to avoid the protracted action of the magnesium sulphate, thus approximating the siphoning out of the solution in the clinical method. In one case where no flow was observed upon opening the duodenum a flow of bile was induced by the application of the sulphate solution. In the other cases an apparent further relaxation of the papillary sphincter and an increased flow of bile into the duodenum was noted. *In no case was any of the methylene blue bile from the gall-bladder seen to appear in spite of the apparent*

stimulation of liver bile. McWhorter[32] had demonstrated a lowering of pressure in the common bile duct of dogs of from 50 to 100 mm. after magnesium sulphate had been applied to the ampulla; no result was seen after peptone solution.

The experiments with methylene blue were controlled by the use of two animals injected with a suspension of carmine powder and one injected with a suspension of pulverized charcoal. In all cases at the conclusion of the experiment the patency of the ducts was demonstrated by exerting very slight digital pressure upon the gall-bladder. This resulted in every instance in the immediate expulsion of the contents of the gall-bladder into the duodenum, staining the mucosa intensely by the methylene blue or producing marked and unmistakable evidence of coloring matter in the cases of the carmine or charcoal suspensions.

Thus it is seen that although the application of magnesium sulphate to the duodenal mucosa at the papilla of Vater has the effect of stimulating bile flow it does not empty the gall-bladder of its contents. The flow of bile direct from the liver indicates that it is not necessary for the bile to go to the reservoir of the bladder before its excretion into the intestine. This experiment further explains the circumstance cited by Hatcher and Eggleston[34] of the rapid recovery of ouabain excreted in the bile in the intestine of a rat within four minutes after completion of injection.

2. *Effect of Substances Other than Magnesium Sulphate.* We wished to ascertain whether the relaxation of the musculature and the flow of bile was due to the specific effect of magnesium as maintained by Meltzer, or whether the salt action of the sulphate radical or any salt itself could produce the same effect.

First, we noted that the application of magnesium sulphate to the duodenal mucosa often produced a local peristaltic contraction of the intestinal wall. If this contraction had been due to the magnesium radical rather than to the salt action, it may perhaps be explained by reference to the work of Ralph Lillie, of A. G. Mayer and of Stockard[48] at the Tortugas Laboratory at Naples about twelve years ago, in which the investigation of properties of Mg, Na, K and other substances showed a contraction of smooth muscle and similar types of cells by Mg, whereas striped muscle showed the characteristic relaxation described by Meltzer.*

* In this connection it is necessary to review the observations of Meltzer regarding magnesium, and to clearly differentiate what Meltzer and Auer[36] actually saw from what Meltzer conjectured. Most of the work of these authors upon magnesium was done either by intravenous injection or by nerve blocking. In the latter set of experiments[46] it was observed that blocking of a peripheral nerve (*e. g.* sciatic) could be brought about by wrapping the nerve in a cloth saturated in strong magnesium solution. In the set of abdominal experiments it was noted[40] that after intravenous injection of magnesium sulphate there was an absence of the violent peristaltic contractions originated by sections below the medulla, by physostigmin or ergot as well as such as are seen as an agonal phenomenon. The only attempts directly to observe the effect of a magnesium salt when applied in the intestinal mucosa is mentioned in the article in the Archives for Internal Medicine.[41] In this article it was noted that

Second, not only was the stimulation of bile flow seen with magnesium sulphate, but a similar increase in biliary excretion was noted after the local application of a solution of peptone, of sodium sulphate, sodium phosphate, bile and sodium glycocholate. No stimulation was seen after the application of sodium choride or potassium or sodium hydroxide.

3. *Contractile Power of the Papillary Muscle.* By drawing the finger over the papilla, by faradic stimulation or by the use of chemical irritants, it was seen in numerous cases that the "sphincter" reacted with a contraction which promptly closed the duct. A high degree of irritability was evidenced, since even the slightest mechanical stimulation sufficed to contract the papilla. An interval of between ten to thirty seconds usually elapsed during which time the muscle of the papilla remained contracted so as to cause a characteristic elevation. Relaxation then took place and the bile flow was resumed. Not only the papilla but the surrounding segment of the duodenum responded to the stimulus. If the stimulus (faradic) was strong enough the whole intestinal segment was tonically contracted.

We attempted in seven cases to cause a contraction of the musculature within the gall-bladder wall by the use of the faradic current, but no success greeted our efforts although we used as many as eight dry cells connected to an inductorium, set to give the maximum stimulus (enough to cause violent tonic contraction of any muscular region to which it was applied on the animal). Thus a current which caused a tonic segmental contracture of stomach or duodenum or small or large intestine failed to evince a response from the gall-bladder.*

peristalsis ceased in a loop of intestine when the lumen was filled with magnesium sulphate solution. It will however be noted that no specific details of such experiments are given, nor can one conclude whether Meltzer regarded such a local intestinal action as due to a nerve block or a direct ionic paralyzant action on the muscle cell. Above all, in view of the great confidence which is justly and properly reposed in all the statements made by the late S. J. Meltzer, it behooves us to remember that he does not at any time quote any experiment in which magnesium was applied to the papilla of Vater; his was a "suggestion," not a "fait accompli." Statements in the literature crediting Meltzer and Auer with having performed any experiments in which magnesium salts were applied to the papilla and its action noted upon either the papilla or the gall-bladder are erroneous. Furthermore, the hypothesis that magnesium sulphate provides its effect upon the bile flow after absorption into the portal or general circulation (Einhorn) is not voided by any experiments of Meltzer and Auer. In fact Meltzer definitely states that magnesium sulphate is readily absorbed from the lumen of the intestine and can by means of the circulation produce its general effect in paralyzing muscular activity.[41] This phenomenon has been studied also by Hertz, Cook and Schlesinger.[47]

* Several physiologists have succeeded in demonstrating that the gall-bladder wall of a dog is capable of giving small rhythmic contractions, both tonal and in response to faradic stimulation. (Doyon, Okada, Burton-Opitz). These experiments were performed usually with a distended balloon in the gall-bladder; such a procedure by stretching or perhaps over-stretching this hollow viscus may likely produce such tonal variations in a smooth muscle organ as to simulate, when recorded upon a kymograph, contractions. To date, however, we believe that no one has seen a gall-bladder actually contract with a forceful constriction of its fibers sufficient to expel its contents.

4. *Nervous Control of Gall-bladder Contractility.* In two instances efforts were made to contract the gall-bladder by stimulation of the vagus and splanchnic nerves. These experiments were not attempts to parallel the work of Doyon or Bainbridge and Dale, but were done merely in our own interest without elaborate preparations such as made by the two authors quoted. (Introduction of balloon and manometer, etc.) In neither case could we excite any visible gall-bladder contraction, although in one case the methylene blue was discharged into the intestine. This, however, we attribute to the fact that strong faradic stimulation of the right vagus nerve caused general abdominal contractions of intestines, diaphragm, stomach, etc., with movement and pressure of the liver and other organs upon the distended gall-bladder. The expulsion of the discolored bile in this case was mechanical rather than nervous.

5. *Gall-bladder Stasis during Normal Activity and Digestion.* Using ether anesthesia, three dogs were operated upon aseptically; the gall-bladders of these animals were injected with suspensions of carmine powder or charcoal. The abdomen was sutured, surgical dressings applied and they were permitted to recover from anesthesia and play about in the animal room. These dogs were fed with fat meat, biscuits and water in order to provide a diet well balanced in protein, carbohydrate and fat. They showed no ill effects upon recovery from the operation and were seen to eat their food with relish. The operations were performed on different days. The animals were permitted to live for twelve, twenty-four and seventy-two hours respectively, at which times they were killed by intracardial injection of a massive dose of strychnin in order to produce immediate death without violent agonal muscular contractions. They were immediately examined and search was made throughout the entire intestinal canal for evidences of discolored bile indicating discharge from the gall-bladder. In none was any trace of carmine or charcoal found. The bile ducts were patent and free from obstruction, as shown by slight digital pressure causing the expulsion of a gush of dye-colored bile from the gall-bladder, unmistakably discoloring the intestinal wall. There was no evidence of any inflammatory lesion or septic condition resulting from the laparotomy or the gall-bladder injection. Active digestion was in progress at the time each of the dogs were killed. No evidence of artificially colored gall-bladder bile was found outside of the bladder itself, although the intestinal wall in the upper region was markedly stained with normal yellow liver bile.

In a further experiment a dog under the same circumstances was observed after the lapse of one week. During the seven days intervening between the operation and the autopsy the dog was fed with a mixed carbohydrate-fat-protein diet. A cutaneous

infection at the site of the incision was observed, but no peritoneal involvement was present.

Examination of the gall-bladder at autopsy showed a normal bladder, half filled with light brown bile and no evidence of the carmine suspension injected a week previously. Examination of the contents and mucous membrane of the colon showed evidences of the carmine powder which had probably been expelled into the intestine one or two days previously. Carmine was not demonstrated in the feces of the terminal colon or sigmoid.

Bile stasis in the gall-bladder of the dog has thus been shown up to seventy-two hours concurrent with active digestion of a balanced diet and with unmistakable evidence of *a free flow of liver bile*. The attempt to extend the observation of this phenomenon to a week showed that by that time the gall-bladder had emptied itself. Apparently there is some sort of uncertain and irregular movement of bile from the sac, though our observations thus far have not confirmed the existence of the supposed ejaculatory mechanism.

6. *Movement of Bile into the Gall-bladder.* In seeking a substance with which to test the movement of liver bile into the gall-bladder we chose phenol-tetrachlor-phthalein, originally studied pharmacologically by Abel and Rowntree[37] in 1909 and described as a test for functional acitivity of the liver in 1913 by Rowntree, Horwitz, and Bloomfield.[38] This substance was freshly prepared in an alkaline solution by boiling under a reflux condenser. On account of experiences with animals which demonstrated to us its toxic nature when given in solutions not sufficiently dilute we administered the dye to chloretonized dogs, by the injection into the femoral vein of 50 cc of a 0.5 per cent solution over a period of fifteen minutes.

A return of the dye in the bile ejected from the papilla was noted usually within ten to fifteen minutes and could be ascertained positively by placing about 1 cm. of the bile collected in a test-tube, diluting with 10 cc of water and then adding a few drops of concentrated sodium hydroxide. The presence of the dye was indicated by the appearance of an intense reddish-purple color. At the same time the dye could be demonstrated in specimens of bile independently aspirated from the gall-bladder.

We repeated the experiments upon a dog, after tying off the cystic duct with a ligature at the neck of the gall-bladder. Injection of the phthalein was accomplished as described above; bile collected from the papilla in fifteen minutes showed the presence of dye being excreted. Periodic aspiration of small amounts of the contents of the gall-bladder were negative for the dye during a two-hour observation period. This showed that phenol-tetrachlor-phthalein was not secreted from the gall-bladder wall.

It further demonstrated that there is an inward flow of liver bile into the bladder.

7. *Filling of the Gall-bladder in a Normal Dog.* An attempt was made to determine the rate of filling of the empty gall-bladder. After laparotomy and duodenotomy the content of the gall-bladder was expressed into the duodenum by pressure upon the organ. The bile continued to flow throughout the period of observation of one hour. The gall-bladder was aspirated by means of a hypodermic syringe at fifteen minute intervals after the digital emptying. In all 7 cc of bile were obtained by this mode of aspiration, 3 cc the first time 2 cc the second and 1 cc at each of the subsequent two aspirations.

The gall-bladder was here seen to begin filling soon after emptying, the rate of filling being, however, very slow.

At a subsequent experiment the same procedure was adopted; in this instance no bile collected in the gall-bladder during a period of two hours, though there was a constant slight flow from the papilla. (These last observations should call for more complete and more numerous investigations.)

Conclusions and Summary. 1. Anatomically the gall-bladder wall contains scanty musculature of poor contractile power.

2. A typical distinct anatomic sphincter at the papilla of Vater was not demonstrated, although there is definite sphincteric action. The papilla shows an extremely high degree of irritability in the chloretonized dog.

3. The nervous control of the gall-bladder is uncertain. We have been unable to produce definite contractions by nervous stimulation and there are conflicting reports of such phenomena observed by others.

4. The application of concentrated solutions of magnesium sulphate to the duodenal mucosa and papilla of Vater of the dog caused a stimulation of bile flow. It did not cause an expulsion of bile from the gall-bladder.

5. The flow of bile into the duodenum is not inhibited by the existence of a fasting state or empty non-digesting stomach.

6. In the fasting state the gall-bladder is not necessarily distended. In the digesting state during copious bile flow the gall-bladder was observed to be filled.

7. Application of magnesium sulphate to the duodenal mucosa caused a stimulation of peristaltic contraction.

8. Bile flow may be induced by the application to the mucosa of peptone, sodium sulphate, sodium phosphate, $\frac{N}{10}$ hydrochloric acid and bile and sodium glycocholate. No stimulation of flow was seen after water, NaCl, $\frac{N}{10}$ NaOH.

9. Strong faradic stimulation of the gall-bladder wall did not contract the organ.

10. Stasis of the gall-bladder contents was observed in normally digesting dogs up to three days. The gall-bladder was found to have emptied itself in one week.

11. The gall-bladder wall does not excrete phenol-tetrachlorphthalein, though the liver does. Although there must be some movement of the bile into the gall-bladder, as evidenced by the presence of this substance in some cases in which the cystic duct was not tied off, how the material passes from the sac and under what conditions is unknown to us.

12. The filling of the emptied gall-bladder is an irregular and a slow process.

Concluding Remarks: After contemplating this series of experiments it would appear that we should reconsider the view of the gall-bladder as an actively functioning organ that rhythmically fills and empties itself under the stimulus of digestion. That the liver bile has normal free ingress into the gall-bladder has been demonstrated. That an enormous inspissation or concentration of bile in the bladder takes place, with the addition of a mucous element, has further been agreed upon and more recently emphasized by Rous and McMaster. But how or at what rate emptying occurs remains open to consideration. Most of the work by physiologists has been done with biliary or duodenal fistulæ; the variations in the bile flow in respect to digestion have been rather presumed to follow and to depend upon the filling and emptying of the gall-bladder.

We are inclined to the belief that the flow of bile originates in the liver and sweeps down the ducts into the duodenum disregarding in main part the gall-bladder. Such variations in bile flow and concentration as occur originate in the liver in answer to the various degrees of food stimuli.

It does not seem that the gall-bladder as an active organ enters into the physiology of bile excretion. Certainly it does not seem to have an ejaculatory mechanism or the proper musculature for such a function in the same light as one speaks of the urinary bladder or of the seminal vesicles. The outflow from the gall-bladder appears to be in the nature of an overflow incontinence. Under pathologic conditions one knows that this organ is capable of great distention, acting at such times as an exhaust vent or safety valve to relieve intraductal pressure. Such a function is complementary to its great capacity to concentrate the bulk of bile by dehydration and inspissation.

REFERENCES.

1. Text-books of Anatomy: Cunningham, Gray, Piersol, Morris.
2. Luschka: Anatomie des Menschen, 1863, **2**, 256.
3. Holmes: Lancet-Clinic, 1911, **106**, 678–684.

4. Oddi: D'une disposition sphinctere speciale, etc., Arch. Ital. de biol., 1887, **8,** 317.
5. Oddi: Monitore zoölogico Ital., 1894, **5.**
6. Hendricksen: Johns Hopkins Hosp. Bull. 1898, **9,** 221.
7. Gay: Trans. Chi. Path. Soc., 1902, **5,** 108.
8. Wilder: History of Human Body, Holt 1909, p. 295.
9. Rolleston: Diseases of the Liver and Gall-bladder, MacMillan, 1912.
10. Oddi: Sul centro spinale dello sphintere del choledoc., Arch. de physiol., normal et path., 1894, p. 931; Sul centro, etc. Lo Sperimentale, 1894, **48,** 180.
11. Doyon: Arch. de physiol. norm. and path., 1894, **6,** 19.
12. Bainbridge and Dale: Jour. Phys., 1915, **33,** 138.
13. Okada: Jour. Physiol., 1914, **49,** 457.
14. Text-books of Physiology: Howell, Starling, Tigerstedt, McLeod, Am. Textbook of Phys., Luciani, Bayliss, Also Barker, Medical Record, 1907, **62,** 555.
15. Mann: New Orleans Med. and Surg. Jour., 1918, **71,** 80.
16. Freese: Johns Hopkins Hosp. Bull., 1905, **16,** 235.
17. Judd and Mann: Surg., Gynec. and Obst., 1917, **24,** 437.
18. Okada: Jour. Physiol., 1915, **50,** 42.
19. Lieb and McWhorter: Jour. Pharm. and Exper. Therap., 1915, **7,** 83.
20. Rutherford: Trans. Royal Soc. of Edinburgh, 1880, **29,** 29.
21. Okada: Loc. cit.
22. Bruno: Arch. d. sc. biol., St. Petersburg, 1899, **7.**
23. Bayliss and Starling: Brit. Jour. Physiol., 1902, **28,** 348; Starling, Human Physiology, Lea and Febiger, 1915, p. 716.
24. Fleig: Arch. internat. d. physiol., 1914, 286.
25. Mann, F. C.: Ann. Surg., 1921, **73,** 54.
26. Hammarsten: Text-book of Physiol. Chemistry, 1904, p. 276.
27. Rosenbloom: Jour. Biol. Chem., 1913, **14,** 24.
28. Rous and McMaster: Proc. Soc. Exper. Biol. and Med., 1920, **17,** 215.
29. Tigerstedt: Lehrb. der Physiol. des Menschen, 1920, p. 389.
30. Hawk: Physiological Chemistry, 1918, p. 207.
31. Meltzer: Am. Jour. Med. Sci., 1917, **153,** 469.
32. Lyon: Jour. Am. Med. Assn., 1919, **73,** 980.
33. McWhorter: Surg., Gynec. and Obst., 1921, **32,** 124.
34. Hatcher and Eggleston: Jour. Pharm and Exper. Therap., 1919, **12,** 432.
35. Dunn and Connell: Jour. Am. Med. Assn., 1921, **77,** 1093.
36. Meltzer and Auer: Am. Jour. Physiol., 1906, **16,** 4.
37. Abel and Rowntree: Jour. Pharm. and Exper. Therap., 1909, **1,** 231.
38. Rowntree, Horwitz and Bloomfield: Johns Hopkins Hosp. Bull., 1913, **24,** 327.
39. Rost: Mitteilung a. d. grenzgb. Med. u. Chir., 1913, **26,** 710.
40. Meltzer and Auer: Am. Jour. Phys., 1906, **17,** 313.
41. Meltzer: Arch. Int. Med., 1915, **15,** 956.
42. Meltzer: Medical Record, (June 7), 1902, **61,** 888.
43. Voit, Carl: Beitr. z. Biol. Festgabe Anat. u. Physiol. Th. L. W. von Bischoff, Stuttgart, 1882.
44. Einhorn: New York Med. Jour., 1921, **113,** 8.
45. Reiss, Crohn and Radin: Jour. Am. Med. Assn., 1921, **76,** 1567.
46. Meltzer: Inhibitory and Anesthetic Properties of Magnesium Sulphate, Med. Rec., 1905, **68,** 965;
47. Hertz, Cook and Schlesinger: Proc. Roy. Soc. Med., 1908, **11,** No. 2; Therap. and Pharm, p. 21.
48. Stockard: Personal communication.

CHEMICAL CHANGES OF THE BLOOD DURING IMMUNIZATION.

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In the present paper the chemical changes occurring in the blood during the process of immunization are considered. In order to make a clear presentation of the subject, it has been found necessary to review in considerable detail some previously published experiments, both our own and those of others. The experiments referred to are studies in carbohydrate physiology, the investigation of which, based upon the microchemical examination of the blood, dates from the work of Jacobsen. Jacobsen[3] found that the ingestion of definite amounts of glucose was followed by a temporary increase in the amount of blood sugar, and that this increase began about 5 minutes after the ingestion, reached its maximum in about 45 minutes and subsided in about 120 minutes. Further studies of this phenomenon made by other investigators[4 5 6 7 8 9 10] have shown that the reaction may be completed in a shorter period of time or may extend over a longer space than 120 minutes and that in some diseased conditions the reaction varies, *i. e.*, the blood-sugar values either rise to a higher level or are less marked than the normal.

Changes in the blood sugar similar to those just described also follow the injection of adrenalin[11] and other internal secretions[12] as well as the injection of protein, peptone and some of the protein-split products,[13 14] certain mineral salts[15] and at least one mineral acid.

Subsequent experiments carried out in this laboratory confirmed the occurrence of hyperglycemia after the injection of peptone and demonstrated that any protein parenterally introduced disturbs the blood-sugar equilibrium,[1] the disturbance manifesting itself by either a temporary decrease or an increase of the blood-sugar concentration. The experiments, furthermore, brought out the fact that similar changes in the blood sugar continue to occur with each subsequent injection of the specified protein (*e. g.*, typhoid bacilli) until the power of the organism to produce antibodies against the protein injected is exhausted, whereupon further injections fail to cause disturbance of blood-sugar equilibrium. It was also found that changes in blood sugar do not follow the subcutaneous injection of autologous protein in normal animals, but do occur when homologous protein is used. This phenomenon

led to the observation that, in contrast to normal animals, about 75 per cent of mice bearing spontaneous malignant tumors fail to show disturbance of blood sugar after the injection of homologous protein.

A protein having been injected into the selected animal the method of determining a disturbance of the blood-sugar equilibrium was as follows.* Just before the injection and again forty-five minutes and one hundred and twenty minutes thereafter, blood was withdrawn and its sugar content determined; the lowest of the three values thus obtained was subtracted from the highest and the

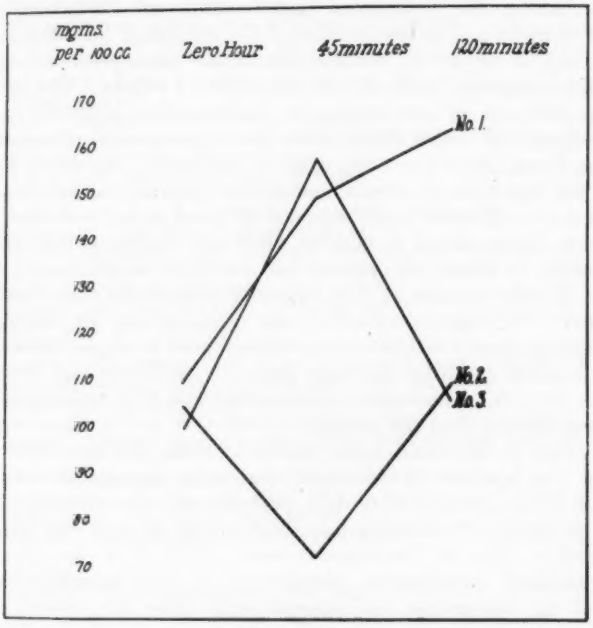

CHART I

variation between these two values represented the disturbance of sugar equilibrium in milligrams. Three methods were used in determining the blood-sugar values in animals, the Epstein, the Kleiner and the Folin (micro). In our hands the Folin method has been found to be the most satisfactory. Inasmuch as in the animal work the comparative but not the actual values are of importance, it is not necessary to use any given method in making the sugar

* In all of our experiments the animals were kept on a fixed diet, and were invariably starved for a period of twelve hours antedating the experiment. They received no food until the last specimen of blood had been withdrawn.

estimations. It is, however, essential that one method be used throughout any one experiment and that all determinations be carefully done by the same person, who should be experienced in blood-sugar work.

In the course of our observations three types of reaction were noted; and while they have been described elsewhere,[8] they are again illustrated in Chart I.

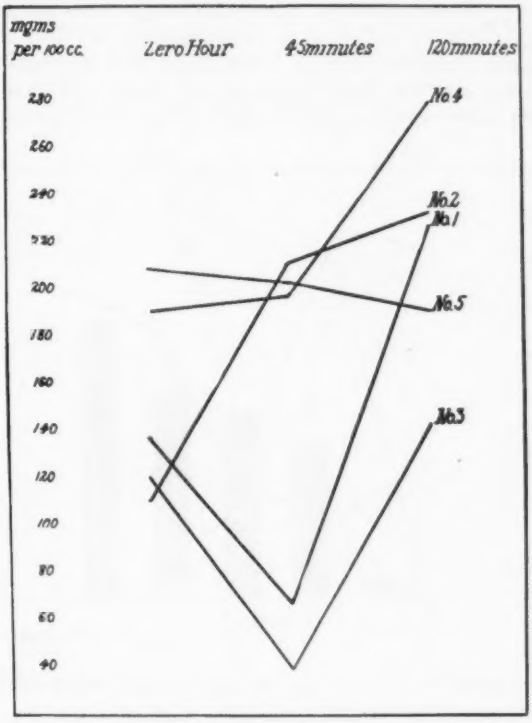

CHART II

Such variations in the reaction must have some significance. It may be, as has been suggested,[16] that in every instance there is an increase in blood-sugar concentration, but that its maximum may occur at different time intervals, and that after the maximum increase there is a lowering of the blood-sugar values below the preinjection value, and finally a return to the preinjection level. In other words, in some instances the reaction is completed very quickly, while in others it occurs slowly. Blood taken at the designated time intervals may, therefore, catch different phases

of the reaction. However, further study of variations in the type of reaction brought out the fact that the same animal, after successive injections of the same protein, reacted differently after each injection, and that the intensity of the reaction also varied. Chart II presents observations on a rabbit injected repeatedly with the same dose of washed sheep red cells. Chart III presents

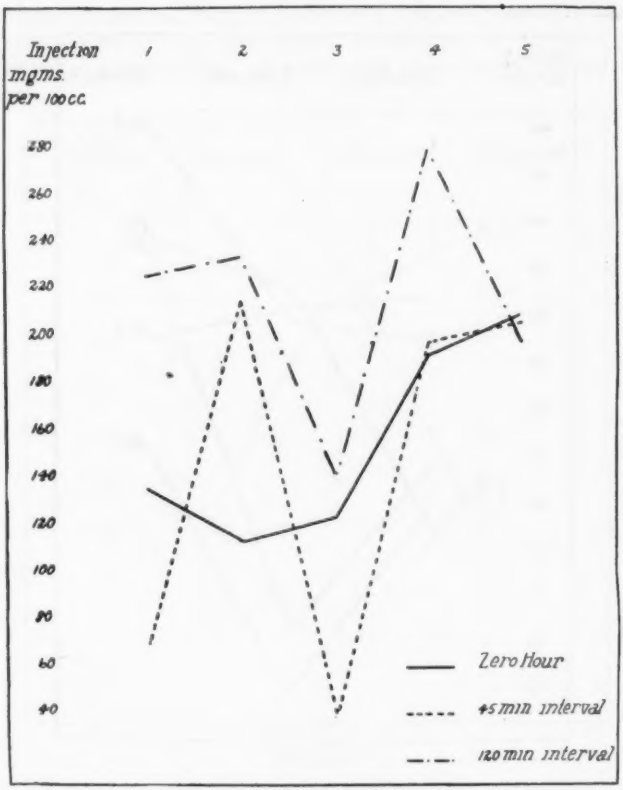

CHART III

the same data in different form. Here the values for the zero hour and the forty-five and one hundred and twenty minute intervals are shown as curves and it is evident that these curves gradually approach one another. In other words, the difference between the high and the low blood-sugar values for each successive test becomes less and less. This successive diminution in the disturbance of the sugar values is striking when presented in the form employed in Chart IV.

In accordance with the foregoing it seems logical to conclude that the disturbance of blood-sugar equilibrium which follows the injection of a protein is not to be judged by the type of reaction but by the degree of disturbance as measured in milligrams.

In view of the disturbances of blood sugar just described it seemed important to undertake further investigations in order to determine if other elements in the blood might not undergo similar disturbances. A further study was therefore undertaken in which the changes in blood sugar, total blood solids, total blood nitrogen and the hydrogen-ion concentration of the blood after protein injection were considered. Particular interest was centered in the possible changes in the total blood nitrogen, since it has been recently suggested [17] [18] that there exist nitrogen-storage centers

CHART IV

analogous to the sugar-storage centers, and it was thought possible that changes in the total blood nitrogen analogous to the blood-sugar changes mentioned in the previous paragraphs might be demonstrated.

Six rabbits, after having been placed on a fixed diet and starved for a period of twelve hours before each test, were injected in varying ways with typhoid bacilli prepared as follows: Three agar slants were incubated for twenty-four hours; each slant was washed off with 3 cc of physiologic salt solution and the suspension was heated to 60° C. for one hour. The injections were made at weekly intervals: Rabbits 1 and 2 were injected intravenously: First dose, 0.5 cc; second dose, 1 cc; third dose 1 cc. Rabbits 3 and 4 were injected intraperitoneally, the doses being

1 cc, 2.5 cc, and 2.5 cc. Rabbits 5 and 6 were injected subcutaneously the dosage being the same as for rabbits 3 and 4.

Just before each injection, and again one hour after injection, blood was withdrawn, and on the specimens so obtained the following estimations were made: Blood sugar by the Kleiner method;[19] total blood nitrogen after the method of Folin;[20] total blood solids as described by Meyers and Fine;[21] hydrogen-ion concentration according to the method of Marriott, Rowntree and Levy.[22] Titers of the serum for agglutinins against typhoid bacilli were also made on blood taken before injection. Before any injections were given, control determinations of sugar, total nitrogen, total solids, hydrogen-ion concentration and agglutinin were made in order to note the changes which would occur in a one-hour interval without the injection of protein.

It will be noted that in this experiment the time periods at which the blood specimens were taken were changed to the zero hour and the sixty-minute interval instead of the previously described three intervals. This was done because interest centered not in the type of reaction encountered, but in the comparative degree of disturbance of equilibrium produced by the injection.

After the last typhoid injection the protein was changed to a 50 per cent suspension of washed sheep red cells in physiologic saline solution. In all the animals the fourth injection, 3 cc of the sheep red-cell suspension was given subcutaneously. The change of antigen was made in order to determine whether, when typhoid antigen had lost its power to induce disturbance of sugar equilibrium, another antigen could still call forth the phenomenon.

The numerical data of this experiment are given in Table I, and these data as averaged for the entire group are graphically shown in Chart V. In general the chemical changes noted were a gradual decline in the concentration of sugar and of nitrogen in all of the animals during the course of the experiment.

A comparison of the behavior of the various fractions of the blood in relation to the development of the agglutinin titer is of interest. The experiment embraces a group of animals subjected to a common type of stimulus. As in all biologic phenomena the individual members of the group have responded in different degree, though not in different manner, to this stimulus. Of the animals injected, two developed agglutinins in increasing strength, two developed agglutinins in increasing strength but very slowly, and two developed agglutinins which reached their maximum with the second injection and then receded. In analyzing a biologic phenomenon in order to determine some broad, general rule, it seems justifiable to consider the experimental group as a whole rather than as individuals, for in no biologic phenomenon with which we are familiar do all of the members of a group necessarily react alike in degree, though they do in manner. For this reason

Animal number.	Dose injected.	Substance injected.	Typhoid agglutinins, titer.	Preinjection.				Postinjection.				Degree of disturbance of equilibrium.			
				Sugar. Mgms.	Nitrogen. Mgms.	Solids. Gms.	Ph.	Sugar. Mgms.	Nitrogen. Mgms.	Solids. Gms.	Ph.	Sugar. Mgms.	Nitrogen. Mgms.	Solids. Mgms.	Ph.
I.	0	0	0	120	2900	17.900	7.0	140	2400	17.890	7.1	+20	500	10	.1
	0.5 cc	Typhoid	400	110	2000	15.600	7.3	110	2100	18.600	6.6	0	100	3000	.7
	1 cc	Typhoid	1800	110	2000	15.700	7.2	100	2000	.....	7.2	−10	0	....	0
	1 cc	Typhoid	2000	90	2100	11.500	7.4	100	2000	16.900	7.4	+10	100	5400	0
	3 cc	Sheep cells	....	60	1900	14.800	7.0	100	1950	15.300	7.6	+40	50	500	.6
II.	0	....	0	120	1900	.....	7.3	100	2000	17.100	7.4	−20	100	....	.1
	0.5 cc	Typhoid	10	80	2000	17.300	7.0	110	2200	18.400	6.7	+30	200	1100	.3
	1 cc	Typhoid	400	90	2000	14.000	7.4	60	2000	13.800	6.6	−30	0	200	.8
	1 cc	Typhoid	1000	100	1900	14.600	7.2	90	1900	14.500	7.2	−10	0	100	0
	3 cc	Sheep cells	....	90	1700	16.900	6.8	90	1700	16.300	7.6	0	0	600	.8
III.	0	....	0	120	2000	17.700	7.3	120	2000	17.100	7.4	0	0	600	.1
	1 cc	Typhoid	0	110	2200	18.000	7.1	110	2200	17.000	7.4	0	0	1000	.3
	2.5 cc	Typhoid	20	110	2000	14.500	7.5	80	2000	15.300	7.5	−30	0	800	0
	2.5 cc	Typhoid	100	100	2100	17.400	7.5	90	2100	16.600	7.5	−10	0	800	0
	3 cc	Sheep cells	....	90	1650	15.300	7.4	120	1600	.....	7.0	+30	50	....	.4
IV.	0	....	0	120	2200	.....	7.1	100	2000	17.000	6.6	−20	200	....	.5
	1 cc	Typhoid	200	70	2000	18.000	6.6	120	2000	20.000	6.8	+50	0	2000	.2
	2.5 cc	Typhoid	1000	90	2000	16.300	7.4	70	2000	17.500	6.8	−20	0	1200	.8
	2.5 cc	Typhoid	500	70	1800	16.300	7.4	80	1800	15.900	7.2	+10	0	400	.2
	3 cc	Sheep cells	....	70	1850	17.600	7.5	70	1860	.....	7.3	0	10	....	.2
V.	0	....	0	100	2300	18.000	7.6	120	2160	18.000	7.4	+20	140	0	.2
	1 cc	Typhoid	0	120	2000	17.000	7.4	90	2000	17.000	6.6	−30	0	0	.8
	2.5 cc	Typhoid	1000	110	2000	17.600	7.3	100	2000	18.000	7.3	−10	0	400	0
	2.5 cc	Typhoid	100	90	1900	15.900	7.8	90	2000	15.700	7.5	0	100	200	.3
	3 cc	Sheep cells	....	70	1700	15.000	7.3	70	1660	16.500	7.7	0	40	1500	.4
VI.	0	....	0	100	2180	19.000	7.1	100	2200	20.000	7.3	0	20	1000	.2
	1 cc	Typhoid	200	120	1900	.....	7.4	130	2000	.....	7.1	+10	100	....	.3
	2.5 cc	Typhoid	200	100	2200	17.000	7.2	110	2200	15.600	7.3	+10	0	1400	.1
	2.5 cc	Typhoid	500	120	1900	16.400	7.8	120	1870	14.500	7.5	0	30	1900	.3
	3 cc	Sheep cells	....	70	1700	15.600	7.4	90	1800	15.500	7.4	+20	100	100	0

All values on 100 cc basis.

the degree of disturbance of equilibrium in any one of the factors which have been considered has been averaged for the entire group. These averaged results are presented in Chart V.

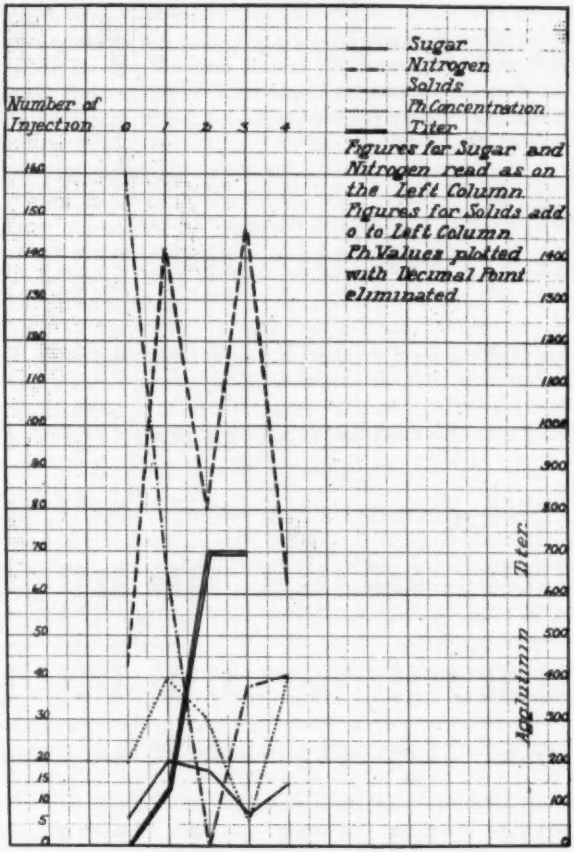

CHART V

Agglutinins. Inasmuch as the experiment was planned to study the relation of various chemical changes in the blood to the development of antibodies the development of agglutinins became the standard of comparison. Before any injections were given, none of the animals had agglutinins for the Bacillus typhosus. Seven days after the first injection the averaged titer was 1 to 135, while seven days after the second injection it reached 1 to 700, remaining at this figure seven days after the third injection;

in other words the maximum agglutinin-producing power of this group resulted in a serum having the power of agglutinating typhoid bacilli when diluted 1 to 700.

Blood Sugar. Control examinations made before any injections were given showed a fluctuation of sugar equilibrium of 6.6 mgm. This is probably not a real disturbance but represents the limit of technical accuracy of the method employed. The first injection resulted in a disturbance of 20 mgm., the second in a disturbance of 18 mgm., the third in a disturbance of 6.6 mgm. At the same time that the titer of agglutinins had attained its maximum disturbances of blood sugar greater than that observed without injection (*i. e.*, greater than the limits of analytical accuracy) ceased. When, however, the antigen injected was changed from typhoid bacilli to sheep red cells there followed a variation of 15 mgm.

Hydrogen-ion Concentration. The disturbances of hydrogen-ion equilibrium are recorded in Chart V only in the first decimal place of the logarithm Ph. As is shown in the chart, these disturbances of equilibrium run parallel to the disturbance of blood-sugar equilibrium. What has been stated concerning the relationship between agglutinin development and blood-sugar equilibrium applies equally well to the disturbances of hydrogen-ion concentration.

Nitrogen. The control examinations (*i. e.*, without injection of any type) made at the designated time intervals showed a disturbance of the total nitrogen equilibrium of 160 mgm. per 100 cc of blood. This is a marked disturbance and cannot be explained by the analytic limitations of the method used. After none of the subsequent injections was there as marked a degree of disturbance of nitrogen balance as was observed without injection, neither was there any demonstrable relationship between disturbance of nitrogen equilibrium and the development of antibodies.

Total Solids. Each injection of typhoid bacilli caused a greater disturbance of the total solids equilibrium than was observed in the control determinations; and in this instance also there was no demonstrable relationship between disturbances of the total solids and the development of antibodies.

The results of the foregoing experiment seem to indicate that while disturbances of the blood-sugar, hydrogen-ion concentration, total nitrogen and total solids do occur with each injection of the protein used, only those of the blood sugar and hydrogen-ion concentration bear any relationship to the development of antibodies.

In a second experiment the work of the first was repeated except for the antibody titration. In this experiment the antigen used was a 50 per cent suspension of washed sheep red cells in physiologic saline, subcutaneous injections, three in number, of 2 cc each, being given. The injections were made at weekly intervals and

three rabbits formed the experimental group. In this experiment, the data of which are given in chart form only (Chart VI) the same cycle was observed as in the first experiment. The disturbances of total nitrogen and total solids equilibrium followed no definite sequence, while the disturbances of equilibrium of both

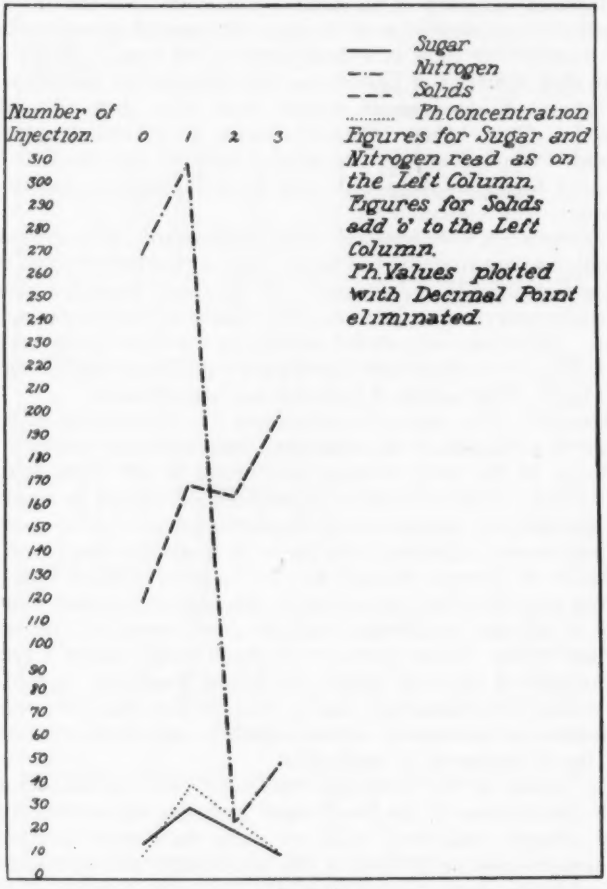

CHART VI

the blood sugar and hydrogen-ion concentration ran parallel and followed a definite sequence.

In a third experiment blood-sugar estimations were made on two rabbits after repeated injections of a 50 per cent suspension of washed sheep red cells in physiologic saline solution. The

injections were given intraperitoneally at weekly intervals and the dose was 2 cc for the first and 3 cc for the subsequent injections. Each animal received seven injections. Lytic titers of the serum were made on specimens withdrawn before the injection of the antigen. The blood-sugar values were determined according

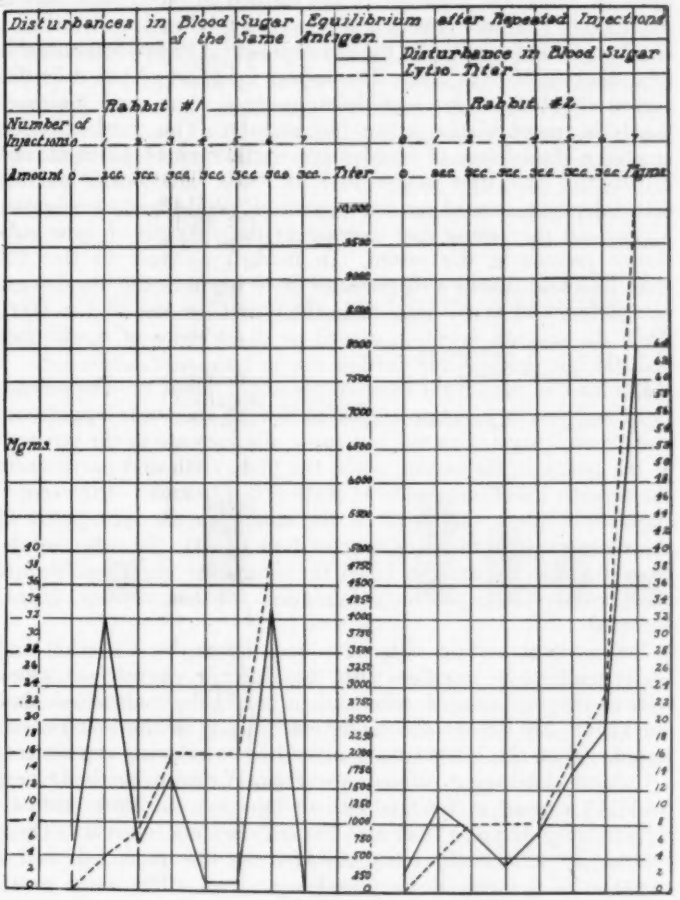

CHART VII

to the micro-method of Folin and Wu,[23] as modified by Wallace and Gallagher,[24] 0.1 cc of blood being used instead of a certain weight, as proposed by Wallace and Gallagher.

The degree of disturbance of sugar equilibrium for each animal is presented in Chart VII, as are the lytic titers for the same animals.

Here the relationship between disturbances of blood-sugar equilibrium and antibody formation is strikingly evident.

Rabbit 1 showed a fluctuation of blood-sugar equilibrium of 3 mgm. before any injections were given. This disturbance is probably not a true one, but, as in our first experiment, represents the limit of analytical accuracy of the method of blood-sugar determination. The first injection of red cells produced a disturbance of 32 mgm. and resulted in the development of lysins demonstrable in a dilution of 1 to 500. The second injection of red cells disturbed the blood-sugar equilibrium only 6 mgm. and increased the lytic power of the serum but slightly. The third injection created a disturbance of blood-sugar equilibrium of 13 mgm. and caused the lytic titer to rise to 1 in 2000. The fourth and the fifth injections created no disturbance of blood-sugar equilibrium, neither did they cause any increase in the strength of lytic substance present in the serum. In marked contrast to this the sixth injection caused a disturbance of 40 mgm. in the blood-sugar equilibrium and at the same time the lytic titer rose to 1 in 5000, while the seventh injection caused no disturbance of equilibrium and did not produce any further rise in lytic titer.

Rabbit 2 ran much the same course as did rabbit 1. The second, third and fourth injections failed to disturb the sugar equilibrium more than 7 mgm., and did not cause any increase in the strength of the lysins in the serum, while the fifth, sixth and particularly the seventh injections produced marked disturbances of the blood-sugar equilibrium, and again at the same time the lytic power of the serum rose to the high titer of 1 to 10,000. In other words, when the injected antigen failed to disturb the sugar equilibrium then no increase in antibody formation (in this instance lysins) occurred.

Inasmuch as certain salts have been shown by Underhill and his co-workers to interfere with the glycemic disturbance which follows the injection of adrenalin, it might be maintained that our results are due to the saline constituents of the material injected. That this is not true is shown by the following experiment:

Control blood-sugar estimations (Folin-Wu micro-method) were made on a group of six rats without injection, the time intervals chosen being the zero hour and the sixty-minute interval. These control determinations, when averaged for the group, showed a variation of 6 mgm. in the blood-sugar level. The same group when injected with 0.5 cc of a mush of rat spleen in physiologic saline solution gave an averaged disturbance of 15 mgm. The same animals were then injected with varying amounts of a saline solution prepared so as to contain the following salts in grams per liter: potassium chloride, 2.062; potassium sulphate, 0.205; potassium monophosphate, 1.202; sodium monophosphate, 0.457; sodium chloride, 3.622; calcium phosphate, 0.193; magnesium

phosphate, 0.177. As is shown in Chart VIII, when this saline solution was injected in the proportion of $\frac{1}{170}$ of the body weight the averaged degree of disturbance was 16 mgm. Such an injection is equivalent to 4230 cc in a 150-pound man. Smaller injections gave progressively less-marked disturbances of blood-sugar equilibrium.

In another series of six rats injections of 0.5 cc of a physiologic saline solution produced a disturbance, as averaged for the group, of 6 mgm. of blood sugar. In the proportion used in our previously described protein experiments, therefore, the influence of the saline solution can be disregarded, because saline injections affect the blood-sugar equilibrium only when injected in a proportion of 1 to 1000 of the body weight or more. The maximum disturbance of blood-sugar equilibrium occurred in the rabbits injected with protein with the initial injection, that is, the one containing

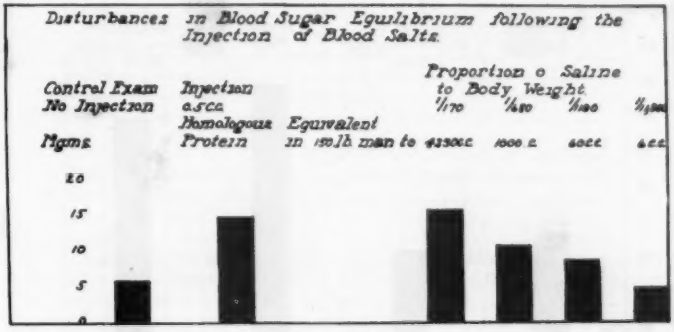

CHART VIII

the smallest amount of saline solution; while later injections which contained larger amounts of saline solution failed to disturb the blood-sugar equilibrium. If the saline were the controlling factor the greatest disturbance of blood-sugar equilibrium would follow the last and not the first injection.

A phenomenon as easily aroused as is the disturbance of blood-sugar equilibrium is probably under a very complex physiologic control, and one is led to suspect the endocrines as regulators.

That the disturbance of blood-sugar equilibrium which follows the injection of protein has a different significance from that of the disturbance which follows the injection of adrenalin is shown by the following experiment:

Sixty normal mice and an equal number of normal rats were injected with 0.125 cc of adrenalin hydrochloride (1 to 1000) solution, blood-sugar estimations (Epstein method) being made just before and again sixty minutes after the injection. An equally large group

of rats and mice bearing transplanted tumors were injected and examined in a similar manner. The averaged degree of disturbance of sugar equilibrium for each group is presented in Chart IX. While mice show a greater disturbance of sugar equilibrium than do rats there is no significant difference between tumor-bearers and normal animals.

When, however, the degree of disturbance of equilibrium following injection of homologous protein is compared in normal mice and in mice bearing spontaneous tumors, it is at once apparent that the disturbance of blood-sugar equilibrium which follows the injection of adrenalin is of different significance from that which follows the injection of homologous protein. In the experiment

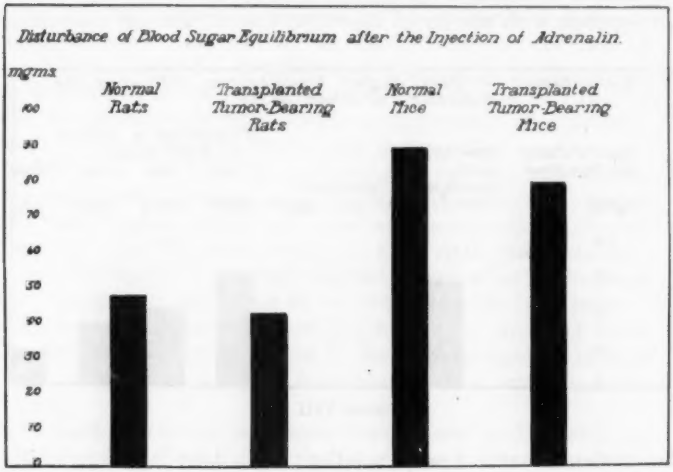

CHART IX

which demonstrates this fact, 28 normal mice and 28 mice bearing spontaneous tumors were injected on different occasions with 0.5 cc of homologous protein derived either from mouse-spleen or mouse-tumor tissue, and on a third occasion were injected with a similar dose of autologous protein derived either from their own spleen or their own spontaneous tumor. Just before and again sixty minutes after such injections blood-sugar estimations were made (Epstein method) and the degree of disturbance of equilibrium estimated in milligrams. The averaged data of this experiment are given in Chart X. It will be noted that autologous protein fails to disturb the sugar equilibrium, for variations of 2 to 6 mgm. are within the limits of analytical error of the method. When

homologous protein is used, however, mice bearing spontaneous tumors react about one-third as strongly as do the normal animals.

That animals bearing spontaneously receding tumors react differently from those bearing growing tumors is shown in another experiment. In this experiment 80 rats, one-half of which carried tumors which subsequently receded spontaneously, while the

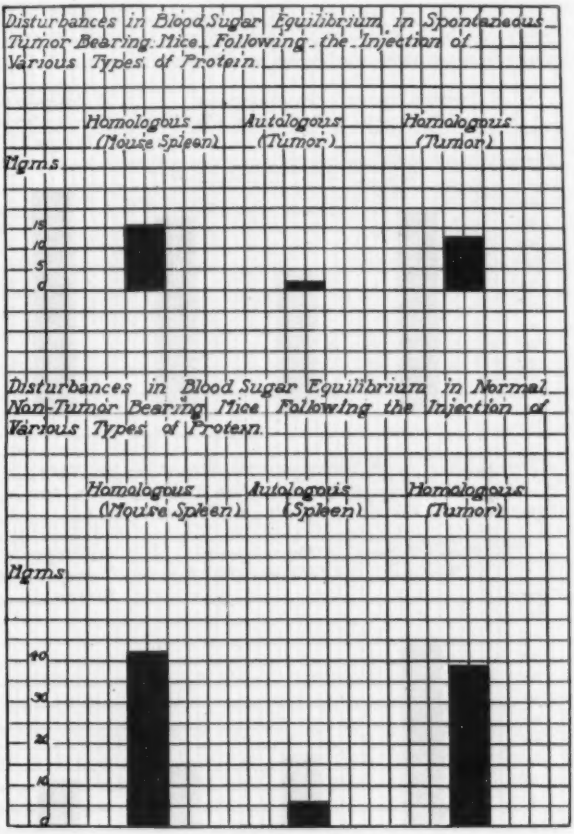

CHART X

other half carried tumors which grew progressively, had their blood-sugar equilibrium disturbed by injection on different occasions of (*a*) 1 per cent solution of heterologous protein; (*b*) two types of homologous protein (rat liver, rat tumor); (*c*) protein from autologous transplanted tumor. The autologous tumor in this instance was the transplanted tumor which they were carrying.

Strictly speaking, however, this is not an autologous protein, for the present host merely furnishes the food supply for a group of cells which have originated in another animal. The averaged data for this experiment are given in Chart XI. Both groups showed the same degree of disturbance of equilibrium after the injection of heterologous protein, the actual values being 46 mgm.

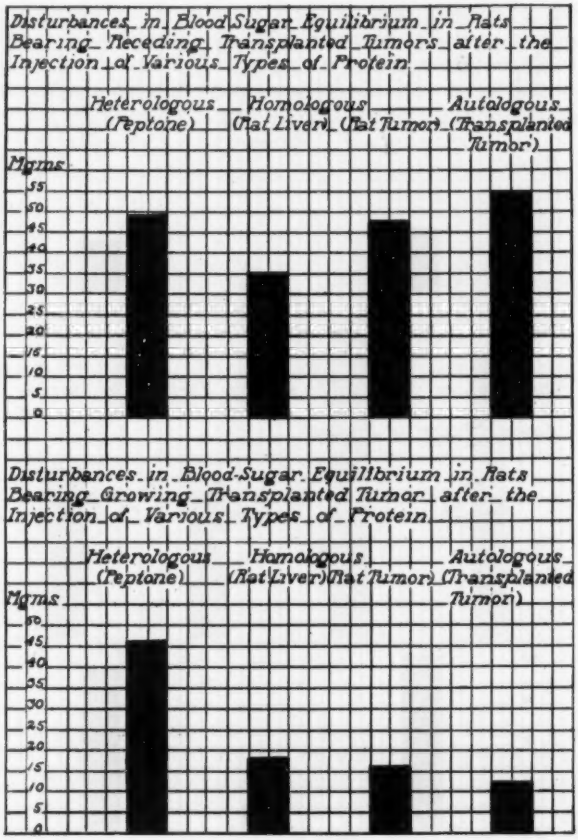

CHART XI

for the progressively growing tumors and 49 mgm. for the spontaneously receding tumors. However, when homologous protein was injected the animals bearing receding tumors showed a greater degree of disturbance than did the group bearing growing tumors, and of the two types of homologous protein used the greatest degree of disturbance of equilibrium was caused by the rat tumor

protein in animals bearing receding tumor. The disturbance of equilibrium in animals bearing progressively growing tumors was approximately one-third as great as that in those bearing receding tumors. The most marked differences between the two groups occurred when the animals were injected with autologous transplanted tumor, for in this instance the animals whose tumors receded reacted approximately five times as markedly as did those whose tumors grew. In marked contrast to the differences of behavior of these two groups when injected with homologous protein is the similarity of their behavior when injected with heterologous protein.

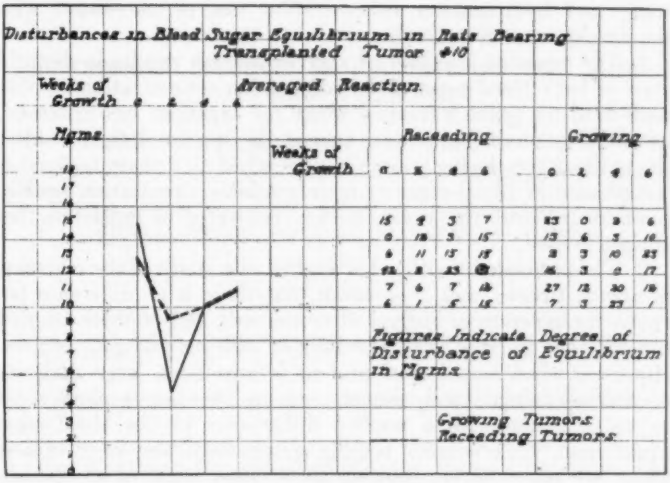

CHART XII

In another experiment the disturbance of blood-sugar equilibrium was studied under somewhat different conditions. Twelve rats were inoculated with rat tumor 10. Just before inoculation and at intervals of two weeks thereafter, for six weeks of tumor growth, blood-sugar determinations were made in these animals just before and again sixty minutes after injection of 0.5 cc of homologous protein (rat spleen); the sugar determinations were made by the modified micro method of Folin and Wu. This tumor strain receded in about 50 per cent of the inoculated animals, and of some 600 spontaneous recessions which have been observed in this laboratory in this tumor strain, 95 per cent have occurred before the fourth weeks of tumor growth.

The data of this experiment are given in detail and in graphic form in Chart XII. It is evident that the group in which the

tumor receded showed a greater degree of disturbance of blood-sugar equilibrium during the period when spontaneous recession most frequently occurs than did the group in which the tumor continued to grow. Interestingly enough, both groups reacted to about the same degree before the inoculation of the tumor, both showed a marked decrease in the reaction at the end of two weeks' tumor growth and both groups reacted to the same degree after the fourth week of tumor growth.

Summary. 1. During the process of immunization there occur disturbances of the total nitrogen content and total solids of the blood, as well as of the blood-sugar and of the hydrogen-ion concentration. None of these disturbances except those of the blood-sugar and hydrogen-ion concentration can be correlated with the development of antibodies.

2. The repeated injection of a given antigen results in disturbance of both blood-sugar and hydrogen-ion concentration equilibrium until the point is reached where the organism has exhausted its antibody-producing powers against the specific antigen. After the antibody-producing powers have reached this phase no further disturbance of blood-sugar or hydrogen-ion concentration equilibrium occurs until the organism has recovered or unless another antigen is used.

3. The principle so outlined is applied in a study of the reactions in animal tumors, and it is shown that there is no difference between the reaction of normal mice and rats and of those bearing tumors when injected with adrenalin or with heterologous protein. However, when homologous protein is injected a large majority of normal animals and animals bearing receding tumors react to the injection with a marked disturbance of the blood-sugar equilibrium, while animals bearing spontaneous tumors or tumors which are progressively growing show either slight or no disturbance of blood-sugar equilibrium.

The application of this principle to the diagnosis of neoplasia in man is considered in another paper.

BIBLIOGRAPHY.

1. Rohdenburg and Pohlman: Am. Jour. Med. Sci., 1920, **159**, 853.
2. Rohdenburg: Jour. Cancer Research, 1920, **5**, 279.
3. Jacobsen: Biochem. Ztschr., 1913, **56**, 471.
4. Hamman and Hirschman: Arch. Int. Med., 1917, **20**, 761.
5. Hopkins: Am. Jour. Med. Sci., 1915, **149**, 254.
6. Taylor and Hutton: Jour. Biol. Chem., 1916, **25**, 173.
7. Janney and Isaacson: Arch. Int. Med., 1918, **22**, 160.
8. Rohdenburg, Krehbiel and Bernhard: Am. Jour. Med. Sci., 1920, **159**, 577.
9. McCasky: Jour. Am. Med. Assn., 1920, **73**, 245.
10. Friedenwald and Grove: Am. Jour. Med. Sci., 1920, **160**, 313.
11. Bloom: Deutsch. Arch. f. klin. Med., 1901, **71**, 146.
12. Achard, Ribot and Binet: Compt. rend. Soc. de biol., 1919, **82**, 788.
13. Kuryama: Jour. Biol. Chem., 1917, **29**, 127, 139.
14. Watanabe: Jour. Biol. Chem., 1918, **34**, 73.

15. Underhill: Jour. Biol. Chem., 1905-06, **1**, 113; 1908, **4**, 395; 1911, **9**, 113; 1911-12, **10**, 159; 1914, **19**, 119; 1916, **25**, 461; 1917, **29**, 127.
16. Geyelin: Proc. New York Path. Soc., 1920, N. S., **20**, 3.
17. Green: Jour. Biol. Chem., 1919, **39**, 435.
18. Moulton: Jour. Biol. Chem., 1920, **43**, 67.
19. Kleiner: Jour. Am. Med. Assn., 1920, **74**, 58.
20. Folin and Farmer: Jour. Biol. Chem., 1912, **11**, 493.
21. Meyers and Fine: Chemical Composition of Blood in Health and Disease, New York, 1915.
22. Marriott, Rowntree, and Levy: Arch. Int. Med., 1915, **16**, 389.
23. Folin and Wu: Jour. Biol. Chem., 1913, **12**, 367.
24. Wallace and Gallagher: Lancet, 1920, **199**, **2**, 784.
25. Rohdenburg and Krehbiel: Am. Jour. Med. Sc., 1921, **162**, 28.

BIOCHEMICAL STUDIES IN DISEASES OF THE SKIN. II. ACNE VULGARIS.

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The theories of the causation of acne vulgaris are many and the remedial agents vary with the underlying notion of its etiology. The very fact that one dermatologist is convinced that it is an infectious disease, that another is certain that endocrinopathy is the causative factor, and that still a third is assured that some dietetic disturbance is responsible, is an evidence that our knowledge of the disease is vague. The changes in the chemistry of the body present in acne vulgaris deserve much study, for it appears to us that until the knowledge of the disturbance in metabolism of this condition is clear and definite, all theories of etiology and all plans of therapy are as fallacious as they are empiric.

It is the purpose of the present communication to summarize briefly the results that we have obtained in the study of some of the metabolic phases of the body in acne vulgaris. The work is still in progress and we hope to throw some more light on the subject in the future.

Nitrogen Retention Products in the Blood. In Table I, it will be observed that the urea nitrogen, non-protein nitrogen and creatinin

content of the blood were determined in 12 cases. In general no abnormal figures were obtained. In those instances in which there were slight deviations from the normal figures, constitutional disorders like exophthalmic goiter and nephritis were found.

TABLE I.—NITROGEN RETENTION PRODUCTS IN THE BLOOD

Case.	Urea nitrogen.	Non-protein nitrogen.	Creatinin.
1	17	24	1.0
2	9	18	1.0
3	9	20	1.05
4	9	24	0.8
5	17	22	0.62
6	26	[illegible]	2.3
7	23	37	2.1
8	11	24	2.8
9	19	23	1.2
10	14	27	1.6
11	14	20	1.5
12	19	23	1.2

Calcium Content of the Blood. One year ago, Thro and Ehn reported that in acne vulgaris the calcium content of the blood (in 12 cases) showed a marked increase, the figures they obtained being from 13.6 mg. to 25.7 mg. per 100 cc of blood. In a previous paper we reported that we had failed to find an increase in the calcium content in the blood from 7 acne patients. At that time we employed the method of Halverson and Bergeim. During the past year we examined the blood from several patients with acne vulgaris for the calcium content by means of the method of Kahn and Hadjopoulus and again found no increase. Recently, Thro and Ehn reported that they found that they had used a faulty method in their previous communication. Upon using another they found quantities of calcium oxide in acne varying from 4.9 to 16.6 mg. per 100 cc of blood. They conclude, "We found that the calcium content of the blood was high in patients with very severe acne who had not been treated, but there were great variations in the amounts of calcium in the blood of acne patients."

The following method of Kahn and Hadjopoulos lends itself to the determination of calcium in small quantities of blood. By the use of this method we found no increase in the calcium content of the blood in acne cases:

To 1 cc of blood serum in a 10 cc test-tube add 4 cc of a 1 per cent solution of ammonium oxalate. Let stand for one-half to one hour and centrifuge for five minutes. Pour off the supernatant fluid. Wash the precipitate three times with distilled water, recovering the precipitate by means of centrifugalization. Add to the sediment 1 cc distilled water and transfer to a vitreosil crucible. The test-tube is washed with distilled water and the washings also collected in the crucible. The water is slowly evapo-

rated and the precipitate burnt in a strong flame until calcium oxide is formed. Dissolve the ash in 0.5 cc fiftieth normal hydrochloric acid with hundredth normal sodium hydroxide, using phenolphthalein as an indicator. The amount of calcium oxide can now be calculated.

TABLE II.—CALCIUM CONTENT OF THE BLOOD IN ACNE VULGARIS

Case.	Mg. CaO in 100 cc.	Case.	Mg. CaO in 100 cc.
1	8.5	9	8.5
2	9.0	10	12.0
3	9.7	11	10.5
4	11.2	12	9.5
5	8.7	13	11.0
6	8.5	14	10.0
7	7.4	15	11.0
8	8.4		

Glycemia. Schwartz, Heimann and Mahnken reported that there is an increase in blood sugar in cases of acne vulgaris. In another communication describing our investigations on the blood chemistry in various skin diseases we corroborated the presence of a hyperglycemia or a high normal blood sugar content in acne. As shown in Table III, we have examined the blood from 34 patients during the postabsorptive period for the sugar content according to the method of Benedict. Out of the 34 specimens examined, 18, or almost 53 per cent, showed figures of 0.1 per cent or more; while 10 of these, or almost 23 per cent, showed figures of 0.12 per cent or more.

Glucose Tolerance. To 24 patients with acne vulgaris on a fasting stomach were administered 100 gm. of glucose in water. The blood was drawn from the vein previous to the administration of the glucose and subsequent to it at two intervals, one of forty-five minutes and the other of two hours. The blood was examined immediately for the glucose content in all these specimens. The results are recorded in Table III.

It will be seen that the glucose curve in all the cases is quite normal. In the average individual there is (subsequent to an ingestion of 100 gm. of glucose) a gradual rise in blood sugar, so that the maximum is attained after forty-five minutes. There is then a gradual decline to normal at the end of two hours. Patients who have a poor tolerance for carbohydrates will, on the other hand, show a continuous rise in the blood sugar with no decline in a period of several hours or days, and the glucose appears in the urine. This latter curve is most suggestive of early diabetes, hyperthyroidism being excluded.

In the series of 23 cases here reported the initial percentage of blood sugar varied from 0.058 to 0.135, rose to a height varying

from 0.08 to 0.17 amd gradually receded to measurements ranging between 0.06 and 0.125, yielding curves corresponding to what we would call the normal.

Renal Glucose Threshold. It will also be observed that 4 of the patients (17, 21, 24 and 29) showed the presence of sugar in the urine subsequent to the ingestion of the glucose. The urine from all the 23 patients was examined for sugar prior to the administration of the glucose and at intervals of forty-five minutes and two hours subsequently. Sugar was absent from all the urines before and after the administration of the glucose, excepting in the specimens from the 4 patients mentioned above. The presence of glycosuria following the administration of 100 gm. of glucose; the presence of a normal blood-sugar curve, and the absence of other symptoms of diabetes warrant a diagnosis of decreased renal glucose threshold.

TABLE III.—GLYCEMIA, GLUCOSE TOLERANCE, RENAL GLUCOSE THRESHOLD IN ACNE VULGARIS

Case.	Glycemia, per cent. Prior to 100 gm. glucose ingestion.	After 3 to 4 hours.	After 2 hours.	Glucose in urine after test.
1	0.1			
2	0.09			
3	0.129			
4	0.13			
5	0.08			
6	0.13			
7	0.17			
8	0.2			
9	0.13			
10	0.1			
11	0.1			
12	0.08	0.088	0.085	0
13	0.08	0.09	0.07	0
14	0.058	0.08	0.06	0
15	0.07	0.09	0.07	0
16	0.08	0.095	0.07	0
17	0.08	0.1	0.09	+
18	0.07	0.15	0.08	0
19	0.06	0.08	0.07	0
20	0.12	0.16	0.09	0
21	0.135	0.165	0.1	+
22	0.07	0.09	0.06	0
23	0.07	0.85	0.06	0
24	0.11	0.17	0.09	+
25	0.06	0.095	0.07	0
26	0.1	0.15	0.1	0
27	0.12	0.17	0.13	0
28	0.09	0.14	0.12	0
29	0.09	0.16	0.1	+
30	0.12	0.15	0.13	0
31	0.11	0.15	0.125	0
32	0.09	0.17	0.1	0
33	0.1	0.13	0.09	0
34	0.1	0.16	0.135	0

Acidosis. In 1919, collaborating with Schwartz and Mahnken, we concluded as a result of investigations as to the alkali reserve of the blood in 139 skin cases that a mild or moderate state of acidosis had been found sufficiently often in acne vulgaris to warrant further study. Sweitzer and Michelson, in 1920, found no marked or consistent change in the alkali reserve in this condition. They employed the Van Slyke method for determining the carbon dioxide combining power of the plasma in 6 cases, and in only 1 was there a mild acidosis. Since then we have continued our studies on acidosis in acne vulgaris in 34 cases.

In this series there was only 1 case which showed a severe acidosis. In this girl the carbon dioxide combining power of the blood plasma was 36 per cent by volume, as determined by Van Slyke's method, and the alveolar carbon dioxide was 4.6 per cent as measured by Fredricia's apparatus. The ammonia output in the twenty-four-hour urine specimen was rather high, 2.74 gm. Ten of the other patients showed a mild acidosis as determined by these methods. Several of the remaining cases showed figures of a low normal alkali reserve of the blood bordering on an acidosis.

TABLE IV.—ACIDOSIS IN ACNE VULGARIS

Case.	CO_2 blood.	CO_2 alveolar Air.	NH_3 gm. 24-hr. urine.	Case.	CO_2 blood.	CO_2 alveolar air.	NH_3 gm. 24-hr. urine.
1	50	...	....	18	56	5.3	1.3
2	54	...	....	19	..	5.2	1.63
3	54	...	....	20	62	5.6	0.95
4	46	...	....	21	..	6.0	0.86
5	40	...	....	22	..	5.8	0.75
6	68	...	....	23	56	5.8	
7	66	...	....	24	54	5.6	
8	54	...	....	25	66	5.8	1.75
9	61	...	....	26	48	5.6	2.23
10	52	...	....	27	50	5.6	1.85
11	48	...	....	28	52	5.8	1.34
12	61	...	....	29	48	5.4	1.27
13	58	5.6	0.94	30	52	5.8	1.65
14	53	5.7	0.11	31	58	6.2	
15	62	5.8	1.51	32	55	5.6	1.53
16	60	5.5	0.82	33	..	5.2	2.25
17	50	5.4	0.82	34	36	4.6	2.74

Studies of the Feces. The stool from 23 patients was examined for enzymes, reaction, fermentation and microscopically for food fibers. It will be seen that most feces were acid in reaction and showed marked carbon dioxide fermentation. Only 4 gave ammoniacal fermentation. The enzymes were excellent in all cases for amylase, were good in all cases save 4 for protease, and were fair or good in all cases for lipase.

TABLE V.—FECES IN ACNE VULGARIS

Case.	Reaction.	Enzymes Amylase.	protease.	Lipase.	Fermentation.	Food.
1	Acid	Good	Good	Good	CO_2	Meat and vegetable.
2	Acid	Good	Good	Good	CO_2	Meat and vegetable.
3	Acid	Good	Good	Good	CO_2	Meat and vegetable.
4	Acid	Good	Good	Good	CO_2	Meat and vegetable.
5	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
6	Alkaline	Good	Poor	Good	NH_3	Much meat.
7	Neutral	Good	Fair	Good	NH_3	Much meat.
8	Acid	Good	Good	Good	CO_2	Meat and vegetable.
9	Acid	Good	Good	Good	CO_2	Meat and vegetable.
10	Acid	Good	Good	Good	CO_2	Meat and vegetable.
11	Acid	Good	Good	Good	CO_2	Meat and vegetable.
12	Acid	Good	Good	Good	CO_2	Meat and vegetable.
13	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
14	Acid	Good	Good	Good	CO_2	Meat and vegetable.
15	Acid	Good	Good	Good	CO_2	Meat and vegetable.
16	Acid	Good	Good	Good	CO_2	Meat and vegetable.
17	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
18	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
19	Neutral	Good	Fair	Fair	NH_3	Much meat.
20	Alkaline	Good	Poor	Fair	NH_3	Much meat.
21	Acid	Good	Good	Fair	CO_2	Vegetable.
22	Acid	Good	Good	Fair	CO_2	Vegetable.
23	Acid	Good	Good	Good	CO_2	Meat and vegetable.

The Basal Metabolism in Acne Vulgaris. Magnus-Levy was the first to point out the theoretical possibilities of metabolimetry in the diagnosis and treatment of constitutional disorders. It remained for DuBois and Benedict and others in this country to succeed in making data concerning the rate of energy production of distinct clinical importance. The term "basal metabolism" designates the heat production of an individual at the lowest level of cell chemistry. The heat production is at its minimum while the individual is at complete mental and physical rest. The most practical method for determining the heat production is by measuring the amount of oxygen consumption by means of a Benedict metabolimeter, and from these data the heat production is calculated in relation to the body surface, which is determined by Du Bois's height-weight chart. The caloric value of oxygen is employed to estimate the respiratory quotient obtained. A variation of 10 per cent from the average is considered within the normal limit.

In view of the fact that acne vulgaris is generally regarded as a cutaneous complication of a constitutional disorder, and considered by some dermatologists as depending for its etiology on an endocrinopathy, we deemed it advisable to determine the metabolic rate in a series of cases. From the data that we have obtained the metabolic rate in the average acne case seems to be enhanced. To incriminate the thyroid from this alone, however, is not justifiable, for the increase in oxygen consumption is very moderate. We hope in the near future to make other endocrine studies with the aim of throwing more light on the subject.

TABLE VI.—BASAL METABOLISM IN ACNE VULGARIS

Case.	Per cent.	Case.	Per cent.
1	+4	12	−3
2	+5	13	+12
3	−3	14	+12
4	+10	15	+10
5	+8	16	+11
6	+9	17	+8
7	+8	18	+9
8	+6	20	+12
9	+14	21	+11
10	+12	22	+8
11	+11		

Summary and Conclusions. 1. We have studied the biochemical status of 38 patients with moderate and severe acne vulgaris of one to fifteen years' duration.

2. In 15 cases in which the nitrogen retention products in the blood were investigated no constant defect could be detected.

3. The calcium content of the blood in our series of cases was not increased.

4. Hyperglycemia, or a high normal blood sugar, accompanied over 50 per cent of the 34 cases studied.

5. The blood-sugar curve was normal in all the 23 patients who were studied for their carbohydrate tolerance.

6. The renal glucose threshold was decreased in 4 out of 23 patients.

7. A mild form of acidosis was found in about 30 per cent of the 34 patients.

8. Feces from 19 out of 23 patients showed carbohydrate fermentation, while only 4 showed protein putrefaction. The enzymes were excellent in all cases for amylase, were good in all cases save 4 for protease and were good or fair in all cases for lipase.

9. The metabolic rate seems to be slightly increased in acne vulgaris.

10. The presence of hyperglycemia and the increased basal metabolic rate seem to point toward dysfunction of the thyroid as a possible causative factor. We believe, however, other glands also are at fault.

11. The following measures have proved valuable in the treatment of this condition: Reduction of the carbohydrates in the diet, gastro-intestinal supervision, administration of alkalies and organotherapy.

12. Thyroid in some cases caused the appearance of increased sympathicotonus and increased the severity of the cutaneous condition; occasionally it seemed to produce involution of the lesions.

13. The administration of ovary, lutein and pituitary has been of benefit in some cases.

THE CLINICAL IMPORTANCE OF ASEPTIC INFARCTION OF THE KIDNEY.

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Infarction of the kidney is a condition more familiar to the pathologist than to the clinician, as the paucity of clinical literature on the subject attests. That knowledge of its manifestations concerns the surgeon was first impressed upon me when I saw two patients suffering with the condition within a period of two months. Both were admitted to the surgical service as cases in urgent need of operation. Schmidt, in his admirable report of three cases from Neusser's clinic, contrasts the frequency of renal infarcts found at autopsy with the rarity of their clinical recognition. He says that the diagnosis is important for differentiation from conditions requiring early surgical intervention.

The following histories of the cases which were encountered illustrate the practical importance of considering the diagnosis of renal infarction in patients with valvular disease who present the symptoms of an acute intra-abdominal disorder.

Case I.—M. Z., male, aged thirty-one years, was admitted to the surgical service on the evening of February 16, 1921, with the following history: Two weeks previous to admission he was suddenly seized with sharp pain in the right lower quadrant of the abdomen. The pain lasted about three hours and disappeared spontaneously. It did not radiate nor was it accompanied by vomiting. Two days later he was seized again with severe abdominal pain, cramplike in character, associated with nausea and vomiting. During the following week he had discomfort in the right lower quadrant of the abdomen, with some temperature, and was confined to bed. Three days ago he left his bed, was seized with violent pain in the left flank and vomited. The pain has been present in this location since the onset. It has been constant in character but intensified by bodily motion and deep breathing. The pain on the day of admission radiated downward to the left testicle. For the past week he has had frequency of urination, voiding about every hour. No dysuria, hematuria, nor pyuria.

Examination soon after admission showed a well-developed, well-nourished man, acutely ill, and apparently in severe pain. Pupils and reflexes were normal, the tongue dry and coated, the breath foul. There was distinct voluntary limitation of respiratory excursions. There were dulness and diminished breathing at the

left base posteriorly, but the lower border of the lung came down with deep inspiration. The heart was somewhat enlarged, the apex-beat was in the fifth space 12 cm. from the midsternal line, where a distinct presystolic thrill was felt. A well-marked rumbling presystolic murmur was heard at the apex and transmitted for a short distance into the axilla. The second pulmonic sound was accentuated. The pulse was 90, regular and of good quality. The abdomen was rigid, specially on the left side. There was tenderness over the left lower ribs in the axilla and in the left hypochondrium below the costal border. There was tenderness in the left costovertebral angle also. The left lumbar muscles were rigid. Rectal examination was negative. Temperature, 101.8°F. Blood count: Leukocytes, 20,000; polymorphonuclears, 82 per cent. Urine on admission: Clear; specific gravity, 1020; albumin present; no sugar. Microscopic examination: A few hyaline casts and occasional leukocytes; no erythrocytes.

The differential diagnosis lay between perinephric abscess, subphrenic abscess, infarction of the spleen and infarction of the left kidney. Because of the repeated attacks of pain, first on the right and then on the left side, and the presence of a definite mitral stenosis and of albuminuria, a diagnosis of renal infarction was made. It was therefore decided not to operate immediately.

Under observation the anterior tenderness and muscular rigidity subsided almost completely. The costovertebral tenderness and lumbar rigidity became predominant. The temperature on the day after admission rose to 103°F. Roentgen-ray examination showed no calculus in any part of the urinary tract. Cystoscopy on February 19 showed no abnormality of bladder or ureteral orifices and no obstruction to ureteral catheters. The indigo-carmine appeared in good concentration in twenty minutes on the left side and in somewhat less concentration on the right side in about the same time. Specimens collected for bacteriology proved sterile. Both specimens showed many granular casts and scattered red blood cells (possibly traumatic in origin). The Wassermann test was negative and the blood culture taken on February 17 showed no growth.

February 19, it was decided to explore the left kidney because of the temperature (102°F.) and the persistent and localized tenderness in the left costovertebral angle. The operation performed by the house surgeon, Dr. Jones, revealed a somewhat enlarged kidney with no gross perinephric changes. The kidney was delivered into the wound easily. It presented at its middle and near the lower pole two grayish-white, pearly, circumscribed areas, about 3 cm. in diameter, firm in consistency with surface slightly above the level of the surrounding parenchyma and a narrow injected zone about each of them. Specimens were removed from these areas for pathologic examination. The kidney was

decapsulated and the wound closed with a small rubber-dam drain behind the kidney.

On the day following the operation the temperature rose to 103.2°F. and then gradually returned to normal by lysis, reaching 99°F. by the rectum on the sixth day. All pain and tenderness disappeared. The urine on the day following the operation showed gross blood, and on the sixteenth day after operation still showed a few scattered erythrocytes. The phthalein test on February 24 showed 15 per cent excretion in two hours, and the blood chemistry on February 22 showed urea nitrogen 37.8, incoagulable nitrogen 77, uric acid 2.6, creatinin 1.4. The tisssue removed at operation proved to be part of an anemic infarct of the kidney. No microörganisms were found in the stained sections.

The wound healed kindly and the patient was discharged free of all symptoms on March 7, 1921, and has remained well up to the present time. Diagnosis on discharge was mitral stenosis and anemic infarcts of the left kidney.

Case II.—J. K., female, married, aged forty-four years, was admitted to the surgical service on the afternoon of April 6, 1921, with the following history: About two hours after eating a light lunch on the day before admission she was suddenly seized with severe abdominal cramps. Toward evening the pain localized in the right upper quadrant of the abdomen, where it became constant and intense, occasionally radiating to the back and shoulders. One-half hour after the onset she vomited. The pain was increased by bodily motion, straining at stool and deep breathing. The bowels moved twice with saline catharsis. The patient had been feverish since the onset. There was no history of previous similar attacks and no urinary symptoms. The patient stated that when nine years old she had chorea which was followed by heart trouble. Since that time she had suffered with palpitation and dyspnea on moderate exertion. About one year ago she had an attack of unconsciousness and aphasia lasting several days, but this cleared up completely. She had several abdominal operations for gynecologic conditions.

Examination showed an obese female acutely ill, cyanosed and dyspneic. She was apparently in severe pain. The pulse was rapid, 120 to 130, and very irregular. The temperature was 102.2°F. The abdomen was moderately distended, but soft, except in the right upper quadrant, where there was a moderate amount of rigidity of the rectus. Marked tenderness was elicited in the right hypochondrium and in the midepigastrium, and slight tenderness in the right costovertebral angle. There was hyperalgesia of the skin in the distribution of the 11th, 12th thoracic and 1st lumbar nerves of the right side. The right lumbar muscles were

rigid. The lungs showed no detectable abnormality. The heart was enlarged toward the axilla, the apex-beat being in the 6th space in the anterior axillary line. Cardiac action was absolutely irregular, but no murmurs could be detected. The pulmonic second sound was accentuated. Blood examination: Leukocytes, 24,000; polymorphonuclears, 91 per cent. Urine: Clear; specific gravity, 1018; large amount of albumin; no sugar. Microscopic examination showed many erythrocytes and but few hyaline and granular casts.

The differential diagnosis lay between acute cholecystitis with possible pancreatitis, acute appendicitis, intestinal obstruction due to postoperative adhesions and infarction of the right kidney. The presence of a cardiac lesion and the urinary findings strongly pointed to the last diagnosis. It was therefore decided to postpone surgical interference.

On the following day the tenderness in the right hypochondrium almost completely disappeared, while that in the costovertebral angle became exquisite. Both conjunctivæ showed a few small recent petechiæ, one in the left conjunctiva showing a prominent pearly central spot. On April 8 all anterior tenderness had disappeared, the posterior tenderness persisting. The phthalein test on April 10 showed 35 per cent excretion in two hours. Blood chemistry on April 7 showed: Urea nitrogen, 33.6; incoagulable nitrogen, 59.5; uric acid, 3.8; creatinin, 1.9; cholesterin, 0.18 per cent. Blood Wassermann was negative. Blood culture taken on April 6 was negative.

With the subsidence of acute pain the temperature gradually fell by lysis, reaching 99.2°F. on the seventh day after admission. The urine continued to show large amounts of albumin, casts and a few erythrocytes until April 18, 1921, when merely a trace of albumin was present and a few leukocytes formed the only abnormal elements. On April 12 the patient was transferred to the medical service of Dr. Libman, who concurred in the diagnosis. On April 13 the blood-pressure was systolic 160 and diastolic 80. The leukocytes were 10,200 with 74 per cent polymorphonuclears. Cystoscopy on April 14 showed no abnormality of the bladder or the ureteral orifices. Good indigo-carmine excretion appeared on both sides in eighteen minutes. Specimens collected for bacteriology showed no growth. During the period of observation of seven weeks on the medical service there was no rise in temperature and no further embolic phenomena. The cardiac irregularity persisted in spite of therapy. The electocardiogram confirmed the clinical finding of auricular fibrillation. The patient was discharged in fair general health with no urinary abnormality except for a faint trace of albumin. Diagnosis: Mitral stenosis and insufficiency, auricular fibrillation and infarction of the right kidney.

It will be noted that these cases have certain features in common. Both patients had mitral valvular disease. The onset in each case was sudden, with abdominal cramps, nausea and vomiting. The pain, then localized to the hypochondriac region, became constant, but was intensified by bodily motion and deep breathing. Tenderness and muscular rigidity predominated anteriorly at first, and later, as the attack subsided, became localized to the lumbar region posteriorly. Albuminuria, cylindruria and erythrocyturia (in one) were present without signs of cardiac decompensation nor the usual manifestations of nephritis. In the absence of pyuria the fever and the marked polymorphonulcear leukocytosis added to the difficulties of diagnosis.

Welch, referring to the question of fever in aseptic embolism, says, "I am not aware of any conclusive observations which show that fever may be produced in this way in human beings." He includes fever, nevertheless, among the general symptoms of renal infarction. Robert Sprinz, in his Inaugural Dissertation at Wurzburg, in 1885, concludes that embolism can produce fever regardless of the nature of the embolized material, and that the fever is due to the embolism, not to the absorption of necrotic tissue from the infarct. Bock has shown experimentally that fever can be produced by the injection into the blood stream of sterile, chemically indifferent particles. Billroth made similar experiments in connection with his studies on wound fever.

Slight fever is noted by Schmidt and Halperin and more marked febrile movement by Riebold. Both Halperin and Riebold report a leukocytosis of over 20,000. The cases here reported show definite febrile movement and well-marked leukocytosis, with all evidence pointing to a bland aseptic infarction.

Senator states that urinary changes occur only with very large or numerous small infarcts and that the presence of blood is essential. Welch, however, says the amount of blood is usually only moderate or even microscopic, and may be absent; hematuria being less common than albuminuria. Chedevergne emphasizes the latter statement in his Paris thèsis, 1901, "De l'albuminurie symptomatique de l'infarction rénal."

Schmidt finds albuminuria constant though transient and erythrocyturia uncommon. In complete unilateral infarction the urine may be altogether negative. The absence of formed elements in some cases may be explained by their retention in the infarcted areas. He emphasizes intense oliguria or anuria in bilateral infarction.

The following abstracts are those of cases reported in the literature, grouped according to etiology.

A. Cases of thrombosis of the renal arteries.

1. Due to trauma.

Von Recklinghausen, 1861.

Boy, aged eight years, died eight days after a fall. Autopsy revealed severe internal injuries. Circular injury to the coat of the left renal artery two lines in length and one in width; ½ cm. below this was a large red thrombus; all branches were thrombosed. The kidney was entirely necrotic.

2. Due to infectious diseases (acute arteritis?).

Juhel Renoy.

A girl, aged sixteen years, recovering from scarlatina. Pain in both lumbar regions on the second day of normal temperature, not severe. Complete anuria for six days; death was preceded by several convulsions.

Autopsy. No cardiac or aortic lesions. Both kidneys were entirely necrosed. Multiple thrombi in the renal arteries and glomerular tufts. Bacteriologic examination negative.

3. Due to subacute and chronic diseases (arteritis, periarteritis).

Halperin, 1908.

In 1905, a man aged forty-two years, was admitted to Micheal Reese Hospital, Chicago. One year ago he had pain in the left big toe after exposure to cold. Five weeks ago the pain recurred and the foot and the lower leg became livid. Gangrene set in and progressed upward. The heart was negative and the urine was normal. Three weeks after admission, fever, sweats, rigors and cough appeared with ascending thrombo-phlebitis of the leg and areas of dulness in the lungs. Urine now showed albumin and casts but no blood. Amputation resulted in recovery.

July 2, 1907. Two weeks' history of pain in the left upper quadrant, vomiting and pain in the left calf. While in the hospital he had two severe attacks of lumbar pain, accompanied by vomiting, headache, fever and leukocytosis of 28,000. Urine: Marked trace of albumin; hyaline, granular and cellular casts, few red blood cells and some hemoglobin. Tenderness in both flanks.

October 6. Severe stabbing pain in the left lumbar region radiating forward to the median line, profuse vomiting and severe headache. The left kidney region was tender. The peripheral vessels were sclerosed. The pain gradually subsided but the urine was suppressed.

October 7. One dram of urine showed much albumin, many pus cells, but no casts or red cells.

October 8. Blood-pressure, 210; temperature, 101°F. Signs of cardiac insufficiency.

October 9. Nine drams of urine obtained showed pus, albumin and hemoglobin. Leukocytes, 16,500; temperature, 99°F. Left kidney explored by Dr. John B. Murphy and found dry, pale gray, practically bloodless.

October 11. Died after six days of almost complete anuria.

Autopsy. Left kidney of normal size showed many cicatricial depressions. In midzone a whitish gray infarct, 7½ cm. in length extending from the cortex to the pelvis and occupying two-thirds of the kidney. The renal artery wall was thickened with a red thrombus at the bifurcation. The right kidney was very small and irregular. There was a large gray infarct of the upper third. There were small cortical infarcts. The renal artery was more thickened than the left, with definite contraction (1 mm. lumen) vessels and branches plugged with adherent red and white thrombi.

Comment. Nationality of patient not given. Microscopic studies of vessels not reported. History suggests thrombo-angiitis obliterans.

Pic and Bonnamour, 1913.

Female, aged sixty-nine years, was admitted February 17 to the Hotel Dieu, Paris, for paralysis of the left face and arm. She presented signs of aortic insufficiency, marked arrhythmia and atherosclerosis. The urine was small in amount and decreasing; there was much albumin.

February 24. Temperature rose to 39° C., when sudden pain in the left flank and abdomen set in.

February 28. Exitus after progressive alleviation of pain.

Autopsy. Dilated atheromatous aorta. Left renal artery and branches completely occluded by a thrombus. Kidney completely infarcted. Pathologist attributed thrombosis to disease of the renal artery and not to embolism.

Manges and Bæhr, 1921.

Man, aged thirty-nine years, was admitted to the surgical service of Dr. Beer, Mt. Sinai Hospital, New York City, June 6, 1919, apparently suffering from some acute abdominal condition. There was a history of cramp-like pains in the calf of both legs radiating to the feet. As these subsided he experienced severe pain in the right lumbar region radiating into the testis, and a few days later had a similar pain on the left side accompanied by hematuria. Six days before admission he had severe epigastric pain, abdominal distention and fever of 102°F. Cystoscopy and the roentgen-ray were negative. Leukocytes, 36,000; polynuclears, 75 per cent. After four days the temperature dropped to normal but leukocytosis persisted. Blood-pressure, 160/90. Blood chemistry: Urea nitrogen, 35; incoagulable nitrogen, 95. Urine negative except for a few red blood cells. P. S. P., 64 per cent.

June 19. Exploration by Dr. Buerger for suspected retroperitoneal abscess revealed periarteritic nodules on the mesenteric vessels. He was then transferred to the medical service, where he developed nodules on the peripheral vessels. In the course of four months he developed signs of progressive renal insufficiency and died of a terminal bronchopneumonia.

Autopsy showed extensive periarteritis nodosa involving many of the small and medium-sized arteries. The most extensive lesions were found in the kidneys. The right kidney showed dense perinephritis, a false aneurysm in the cortex, occlusion of nearly all the renal arterial branches by thrombi. The left kidney was small, its surface studded with large depressed scars the result of numerous old infarctions, and its vessels extensively diseased. The cortical markings were completely obscured in both organs.

B. Cases of embolism of the renal arteries:

Traube, 1853.

Machinist, aged eighteen years, with aortic insufficiency.

October 14. At 1 A.M., sudden onset with pain, awoke from sleep. Pain intensified by pressure over the right kidney, by bodily motions and cough; lessened by lying on the right side and by leeching. It radiated into the right thigh. The urine before the attack was small in amount dark and sedimented. After the attack it was diminished in amount and was dark, with uric acid sediment but no albuminuria. Pressure sensation in the bladder region, dysuria, increased pulse-rate and restlessness.

October 19. Vomiting and collapse, fear and restlessness and air hunger. Died nine days after onset.

Autopsy. The aortic valves were incompetent, with warty vegetations. Splenic infarct the size of a hazelnut. Old small infarcts of both kidneys, but the right showed a large infarct extending from the convex border to the pelvis, two inches long and prominent.

Bartels, 1870.

Boy, aged eight years, previously tracheotomized for croup, suddenly developed pain in the region of the spleen, which became enlarged. Several days later pain in the left thigh, followed by paresis of the extremity and death in four days. There were no urinary symptoms.

Autopsy. Large splenic infarct. Large left renal infarct; renal capsule and perirenal fat thick and swollen. The renal artery and its branches were thrombosed. Healing lesions of diphtheria. Thrombus in the apex of the left ventricle, with ragged, broken surface (probable source of emboli).

Von Leube, 1895.

Cabinet-maker, aged seventeen years. Acute endocarditis (aortic insufficiency) in the course of acute articular rheumatism. The patient's urine contained albumin and blood. The left kidney region was very tender. No edema. Blood disappeared in two days and the albumin in six days. On March 6, pressure in the chest, headache, and fever of 38.6° C. appeared. The urine again showed

albumin and blood and the left kidney again became tender. Urinary changes persisted seven days, then all the symptoms subsided. Diagnosis of renal infarction was made. The patient recovered.

Chedevergne, 1902.

Male, aged twenty-two years, with aortic and mitral disease. Urine negative over long periods of observation in two hospitals. Returned six days after discharge with marked dyspnea and arrhythmia but without passive congestion. Urine now showed a large amount of albumin without casts. Sudden pain in the popliteal space of the right leg. Urine decreased in amount without increased concentration; the albuminuria increased. Gangrene of the right leg at first dry, then moist supervened, and death ensued with septic phenomena.

Autopsy. Mitral stenosis and secondary insufficiency of the aortic and tricuspid. Kidneys showed several deep depressions. The left kidney showed a recent infarct the size of an olive. The right femoral artery was occluded.

Schmidt, 1901.

Laborer, aged forty years; had rheumatism, pleuritis and carditis four years ago.

September 25. The patient was admitted with dyspnea, cyanosis and venous engorgement of the lungs and the liver.

October 10. Sudden pain in the right flank, increasingly intense.

October 11. Tender in the right lumbar region posteriorly and under the liver anteriorly; vomiting, hiccough, constipation.

October 13. Pain was aggravated by motion, breathing, vomiting, etc., and was relieved by lying on the affected side.

October 14. Pain disappeared but the lumbar tenderness persisted.

October 17. Peritoneal friction rub was felt anteriorly below the liver. The urine was not diminished; no changes. No fever. Sudden exitus the next day.

Autopsy. Healed endocarditis of the mitral valve. Extensive anemic infarct of the right kidney with hemorrhage into the renal capsule.

Schmidt.

Female, aged twenty-one years, had recurrent polyarthritis with cardiac involvement. Two years ago had hemiparesis, which gradually cleared up.

December 16, 1899. Admitted, complaining of anorexia, attacks of dizziness, headache and precordial pain. Findings, delicate individual, with slight flush and cyanosis. Mitral stenosis and insufficiency. Urine: 1022; amount, 1000 cc. Nucleo-albumin + serum-albumin—No fever.

February 26, 1900. Discharged improved.

November 6, 1900. Readmitted, with slight edema of the legs.

December 2. Severe pain in the gall-bladder region, radiating to the lower thorax and flank; incessant vomiting and marked dyspnea; tenderness in the right flank.

December 3. Similar attack on the left side. Pain was relieved by lying on the belly, but was increased by deep breathing and movement of the right hip.

December 4. Almost complete suppression; hiccough; constipation; comfortable only with knees flexed.

December 6. Retention and oliguria; obstipation; headache; hiccough.

December 7 to 9. Rentention and oliguria persist. Gastrointestinal disturbance continued.

December 16. Progressive loss of weight and strength.

December 21. Exitus.

Highest temperature was 39° C. (December 4). There was one chill.

(December 5). Urine was entirely negative before the attacks. After the attacks there was marked oliguria and albuminuria, with red bloods cells. No casts or renal elements.

Autopsy. Healed mitral lesion with lime deposit. Numerous infarcts of the kidneys, specially the left. Numerous large infarcts of the spleen.

Schmidt.

Man, aged forty-five years, with mitral stenosis and insufficiency, who had responded to digitalis in several periods of decompensation.

December 6, 1901. Sudden attack of pain in the right upper abdomen with vomiting, dizziness and collapse. Pain localized to the right kidney region a few hours later.

December 7. Similar pain but less severe in the left kidney region. The pain was deep seated, constant and made worse by bodily motion and deep breathing. Tender to percussion over both kidneys and to pressure anteriorly below the costal border. Anorexia, vomiting and constipation, which persisted four days. Ileocecal region was tender. Great difficulty in voiding.

December 10. Leukocytes, 11,000. Temperature, 38.3°C.

December 16. Apparently well.

December 17. Epileptiform seizures followed by coma. Signs of right hemiplegia. Pulse in the left radial and brachial regions disappeared. Exitus.

Urinary changes were of interest. Oliguria with onset of renal infarction. Postembolic polyuria hitherto unobserved was noted. Only a few red cells were in the sediment. Definite albuminuria.

Epithelial casts of polygonal cells with red cells attached to each cast were found.

December 6, 7, 8. Casts of brownish color covered with urate, waxy-like casts and a few free red blood cells.

Autopsy. Old double mitral lesion, thrombus in the left auricle, multiple anemic infarcts of both kidneys. Infarcts of spleen. Embolus in the left Sylvian and left brachial arteries. Erosions of gastric mucosa.

Riebold, 1905.

Housemaid, aged twenty-nine years, suffering with cardiac decompensation and irregularity, the result of rheumatism seven years previously. Mitral stenosis and insufficiency. Improved under digitalis.

October 11. Sudden severe pain in the left flank, with nausea, vomiting and collapse. Pain constant, localized, aggravated by bodily motion and deep breathing. Abdomen distended, tender, specially in the left upper quadrant, with marked skin hyperalgesia. Marked constipation, no passage of gas. Temperature, 37.6° C.

October 12. Continued vomiting and pain. Spleen enlarged. Retention, but catheter yielded 500 cc of normal urine. Leukocytes, 21,600; temperature, 38.9° C.

October 13. Less pain, no vomiting, but obstipation with tenderness in the left upper quadrant.

October 14. Bowels moved and urine voided, but severe pain reappeared in the left flank and also appeared in the right flank.

October 16. Sudden right hemiparesis.

October 17. Exitus.

Autopsy. Left kidney; upper half completely infarcted, multiple small infarcts in the lower half. Perirenal tissue thick and edematous. Embolus lodged in the renal artery. Right kidney: Two cherry-sized fresh infarcts. Spleen: Wedge-shaped anemic infarct, the surface of which showed fibrinous exudate. Embolism of the basilar artery. Double mitral lesion.

Von Jagic, 1915.

Female, aged thirty-nine years, with postrheumatic cardiac disease; two weeks prior to admission, February 10, 1914, had an attack of pain in the left side of the abdomen, cramp-like and persistent. She presented signs of mitral and tricuspid disease, marked abdominal distention, with tenderness in the left lower quadrant, but no rigidity or rebound sign. Evening temperature, 39.2° C. Urine: 500 cc; specific gravity, 1023; much albumin, no blood. After three or four days there was a subsidence of pain and temperature.

February 14. Sudden rise in temperature to 38° C.

February 16. Repeated vomiting and severe pain on the right side, and a tender mass below the costal border.

February 27. Sudden exitus.

Autopsy. Mitral and tricuspid stenosis. Thrombi in the left auricle and ventricle. Emboli in both renal arteries, with anemic infarction of large areas of parenchyma.

C. Cases of doubtful etiology.

Gayet and Favre, 1914.

Female, aged thirty-four years, had typhoid with albuminuria in 1904. Vague renal pain simulating stone colic appeared in 1908. In 1913, urinary symptoms and attacks of colic led to cystoscopy. The right kidney function was half that of the left, some pus and colon bacilli. Roentgen ray was negative.

January, 1914. *Operation.* Right nephrectomy. Kidney showed infarct of half the kidney with small calcific lesion at the center. Was it due to typhoid or was it a sclerocyst about a small calculus?

Rathbun, 1916.

Russian teamster, aged thirty years, noted frequency and urgency of the urine one and a half years ago. One year ago had dull pain in the left flank with radiation along the ureter, growing progressively worse. The left kidney was palpable and tender to pressure and percussion. All examinations were negative. Equal and good excretion of P. S. P. from the kidneys. Congestion of the posterior urethra was relieved by treatment, but lumbar pain persisted.

May 5, 1916. *Operation.* Kidney enlarged and showed several hard lumps. Organ split and four lumps of fibroid consistency noted. Kidney had to be removed later for hemorrhage, and lesions were found to be infarcts with plugged vessels and coagulation necrosis. The patient had no cardiac lesion. No abnormality of urine was detected preoperatively.

Comment. Note strong resemblance to pseudogummatous lesions described by Beriel and Devic (les sequestres des reins).

Etiology. The immediate cause of renal infarction is the shutting off of the blood supply to smaller or larger areas of parenchyma. This may be due to thrombosis in the renal artery or its branches brought about by trauma, acute arteritis in the course of an infectious disease, chronic arteritis, atherosclerosis or periarteritis nodosa. Embolism is a more common cause of infarction. Chronic valvular disease was the cause of embolism in 10 cases, of which 2 were aortic and 8 mitral. The mitral lesions were stenotic and in 2 thrombi were found in the left auricle. The problem of embolic phenomena in valvular disease has been studied by Libman in connection with subacute bacterial endocarditis in the healing

or healed stage. In his opinion valvular defects *per se* do not provide emboli which produce clinically recognizable phenomena. When such phenomena do occur in patients with chronic valvular disease and bacteria-free blood the presumption is strong that the rheumatic infection has been followed by a bacterial invasion which has gone on to spontaneous healing.

It is important to remember that while infarcts occurring in the active bacterial stage of the disease do not suppurate, nevertheless the emboli producing these lesions are not aseptic.*

Aseptic emboli may come from thrombi in the pulmonary veins or the left auricle; from atheromatous lesions, ulcers, fibrinous deposits, thrombi or calcified vegetations on the mitral and aortic valves, or from atheromatous lesions of the aorta. Paradoxic emboli passing from some peripheral vein through an open foramen ovale or open septum may produce infarction.

Such conditions as aneurysm of the renal artery, thrombosis of the renal veins and infarction of the renal cortex in eclampsia do not come within the scope of this paper, as their clinical manifestations are different.

Onset. In the cases associated with chronic valvular disease the onset is sudden with severe pain in the abdomen and flank accompanied by vomiting, fever and more or less prostration and signs of collapse. In a few cases there was a history of mild indefinite attacks on the same or opposite side.

Pain. The first symptom is sudden, severe pain referred to either hypochondrium below the costal border or even to the lower quadrants of the abdomen. It is maximum at onset, constant not colicky, and variously described as cutting, pressing or burning. Morphine is required for its relief. It is intensified by deep breathing, coughing, retching, straining at stool, by bodily motions and extending the thighs. It is lessened by lying on the affected side and flexing the thighs. In a bilateral case the patient may lie on the belly to obtain relief.

As the pain diminishes, in the course of twenty-four hours, it tends to localize to the lumbar region posteriorly. In some cases the pain is referred to the back and flank from the outset. Radiation to the thigh and to the testicle occurred twice.

Tenderness and muscular rigidity are chiefly anterior at first and strongly suggest some acute intraperitoneal disorder. Lumbar percussion, however, causes pain from the beginning. As the acute pain of onset subsides the anterior tenderness and rigidity diminish, costovertebral tenderness and lumbar rigidity become predominant.

According to Schmidt the pain is due to three factors: Increased intracapsular pressure, damage to the renal plexus along the vessels

* Jurgensen's case, Nothnagel's Handbuch, **15,** 105, has been excluded because it probably belongs in this category.

and perinephritis. Localization depends on the position of the kidney and the nerve trunks affected. Thus the areas of skin hyperalgesia correspond to the 11th and 12th thoracic and 1st lumbar nerves, and pain may occur in the distribution of the iliohypogastric nerve. Perinephric hemorrhage, edema or thickening are noted in four autopsies.

Associated Vascular Phenomena. In 2 cases there was a history of cerebral embolism producing aphasia in one and hemiparesis in the other, both having completely cleared up. One of my cases had conjunctival petechiæ. Splenic infarcts occurred in 5 cases. Embolism of the femoral, brachial, Sylvian and basilar arteries with their resultant disturbances were also noted in the course of the disease. In the case of chronic endarteritis of the renal vessels (Halperin's case) there was a preceding gangrene of the leg due to disease of the vessels. The case of periarteritis nodosa naturally presented widespread vascular lesions and their effects.

Fever and Leukocytosis. These have been discussed in preceding paragraphs.

Urinary Symptoms and Changes. Bladder function was disturbed in 5 cases; in 1 there was frequency and urgency, in 1 dysuria, in 1 there was great difficulty in voiding, and in 2 there was actual retention. In 3 cases no urinary changes were observed. Marked diminution of urine was noted in 5 cases and complete or almost complete suppression occurred in 2. Albuminuria was present in 9 cases to a marked degree and constituted the most frequent urinary abnormality. Macroscopic hematuria occurred only in the case of periarteritis nodosa, and contrary to the usual belief was not a part of the clinical picture. Erythrocytes were present in 6 cases, and in 6 their absence was specifically recorded. Casts, hyaline, granular or cellular, were present in only 4 cases.

Gastro-intestinal Symptoms are prominent in the clinical picture. Nausea and vomiting at the onset, often persistent and incessant, abdominal distention, constipation or even obstipation, together with the referred pain, tenderness, rigidity of the abdominal muscles, fever and leukocytosis strongly incline one to suspect some acute intraperitoneal disorder requiring immediate surgical intervention. These symptoms are of reflex origin at first and toxic or suburemic afterward.

Diagnosis. To establish a clinical diagnosis of aseptic renal infarction we must find a source for an aseptic embolus (usually valvular disease) or evidence of some constitutional or vascular disease which can produce thrombosis in the renal vessels. In cases of valvular disease we must exclude active bacterial forms of endocarditis. Of the symptomatology emphasis should be placed upon the sudden onset with abdominal pain and gastro-intestinal disturbances. It is characteristic for the pain to be anterior at first and to localize to the kidney region later. Lumbar

percussion, however, elicits pain from the beginning and costo-verebral tenderness persists after spontaneous pain has ceased. While urinary abnormalities are not constant the presence of albumin and erythrocytes is confirmatory.

Differential Diagnosis. The conditions with which renal infarction may be confused have been indicated in part. The most important is that group of intraperitoneal disorders which requires surgical intervention, namely: Appendicitis, cholecystitis, intestinal obstruction, mesenteric vascular occlusion, perforative peritonitis. A second group of cases is that resulting from obstructive lesions in the ureter occasioned by the presence of or passage of a calculus, blood-clots, inflammatory, leukoplakic or tumor tissue, or by angulation, spasm or inflammatory swelling of the ureter. A third group of cases is that in which renal pain results from sudden increase of intracapsular pressure without obstruction in the urinary passages. Such would be produced by torsion of the vascular pedicle of a floating kidney, compression of the renal veins by retroperitoneal hematomas or inflammatory processes, hemorrhage or congestion in a renal neoplasm. Exacerbations in chronic inflammations of the kidney, as in so-called nephralgie hematurique, produce a similar condition and are specially difficult to differentiate. The renal congestional colics occurring in connection with menstruation as described by French authors also belong in this group.

Schmidt gives a very complete discussion of the details of differentiation.

Prognosis. Of the cases collected, Leube's and my own recovered. The 2 cases of doubtful etiology and pathology recovered after nephrectomy. Bilateral renal infarction occurred in 7 cases, in 5 of which marked suppression or anuria resulted in death. Other embolic lesions appeared to have caused death in 4 cases. In 1 unilateral case the cause of death is not clear; in 1 suppression occurred. Although a patient may recover completely from an attack of renal infarction the underlying disease places him in constant danger of subsequent attacks and of other more serious embolic or thrombotic accidents.

BIBLIOGRAPHY.

1. Bartels: Untersuchungen über die Embolische Processe von Dr. J. Cohnheim, 1872, p. 77.
2. Beriel and Devic: Lyon méd., 1913, **120,** 1263.
3. Billroth: Arch. f. klin. Chir., 1872, **13,** 579.
4. Bock: Arch. f. exper. Path. u. Pharmakol., **68.**
5. Chedevergne: Paris Thèses, 1901–2, No. 375.
6. Gayet and Favre: Lyon méd., 1914, **122,** 349.
7. Halperin: Arch. Int. Med., 1908, **1,** 320.
8. von Jagic: Wien. med. Wchnschr., 1915, **65,** 290.
9. Juhel Renoy: Traité de médecine (Charcot, Bouchard et Brissaud), **5,** 643.
10. von Leube: Specielle Diagnose der inneren Krankheiten, 1895, p. 341.

11. Libman: Am. Jour. Med. Sc., 1913, **146,** 625. Med. Clin. of North America, 1917, **1,** 573.
12. Manges and Baehr: Am. Jour. Med. Sc., 1921, **152,** 182.
13. Pic and Bonnamour: Lyon méd., 1913, **120,** 1306.
14. Rathbun: New York Med. Jour., 1916, **104,** 734.
15. von Recklinghausen: Virchow's Arch. f. path. Anat., 1861, **20,** 205.
16. Riebold: Deutsch Arch. f. klin. Med., 1905, **84,** 498.
17. Schmidt: Wien. klin. Wchnschr., 1901, **14,** 451 and 486; 1902, **15,** 643.
18. Senator: Die Erkrankungen der Nieren, p. 131.
19. Sprinz: Inaugural Dissertation, Wurzburg, 1885.
20. Traube: Ueber den Zusammenhang von Herz und Nierenkrankheiten, 1856, p. 77.
21. Welch: Allbutt and Rolleston's System, **6,** 742, 762, 803.

THE STUDY OF VESTIBULAR NERVE FUNCTION IN MYXEDEMA.*

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The study of the phenomenon of lowered irritability was suggested by the occasional finding of nerve deafness in certain myxedematous patients. As we know, myxedema, or hypothyroidism, is a condition arising from dysfunction of the thyroid gland and manifesting itself by change in weight, cardiac disturbances, dry skin, and other visceral upsets, associated with a certain slowness in response to external stimuli.

From time to time additional data have been added to our knowledge of the interesting condition of myxedema. In recent years light has been thrown on the clinical picture of the condition by the work of Plummer, and Boothby and Sandiford, along the lines of the basal metabolic rate. This work, in conjunction with the isolation of the active principle of the thyroid gland by Kendall, has been of inestimable value in the manipulation of such cases. The literature on the subject has been well combed and brought to date by Lisser, who discusses at length the various changes in the special senses in cretins and in myxedematous patients. St. Lager has reported 5000 cretins in Switzerland and 4000 deaf mutes; 80 per cent of the latter were cretins. Scholz found that 29 per cent of cretins were deaf mutes and that 32 per cent of the others were hard of hearing. Hammerschlag, who was one of the first carefully to investigate the condition, found peripheral ear changes and disturbances in the bone conduction. Various theories and hypotheses have been advanced with regard to the changes taking place, such as ossification of the stapes, impaired development of the epithelial cells in the ductus cochlearis, and so forth. In cases in which the thyroid gland has developed a dysfunction after

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puberty, marked disturbances of hearing are found which can readily be distinguished from the endemic variety by the rapid and spectacular improvement following thyroid therapy.

Lisser calls attention to the fact that Wagner supposed the impairment in hearing was due to myxedematous swelling of the mucous membrane of the middle ear, but Denker found that in thyroidectomized dogs, that had become entirely deaf after operation, there were no histologic changes of a myxedematous character, and stated that the question remained unsettled. It was this statement that prompted me to investigate, clinically, the eighth nerve tracts by equilibration tests.

The literature on the subject of myxedema, which is most voluminous, constantly directs attention to the fact that such patients complain of deafness and tinnitus, but nowhere in the available literature have I been able to find a single reference based on the function of the eighth nerve tracts as demonstrated by the Bárány tests. While the results of my investigation may not be of paramount value in themselves, they are nevertheless an additional bit of datum to the sum total of recorded findings.

Fifteen cases of myxedema were studied; these had been definitely diagnosed as such by the clinical findings in conjunction with the various laboratory tests, most noteworthy of which is the determination of the basal metabolic rate. I shall not dwell on the various changes, such as dry skin, lack of perspiration, and so forth, or quote profuse statistical material which in itself is more or less confusing, but shall make a preliminary report on the cases studied thus far. The equilibration test was made at about the same time the basal metabolic rate was taken. Some of the patients were placed on thyroid therapy and have reported their improvement by proxy. Except in one or two instances they have not as yet been tested to note the improvement, if any, in the eighth nerve tracts.

SUMMARY OF CASES.

CASE 1 (200923).—Mrs. R. O. L., aged forty-nine years, came for examination, July 14, 1917, complaining of indefinite gastric symptoms and increased weight. The general examination was negative. February 28, 1918, the metabolic rate was taken and found to be −17 per cent.

The hearing test showed a slight nerve involvement such as is seen with edema of the internal ear. The equilibration test showed a definite reduction in irritability, especially on the left side. The reduction was most marked in the reaction time.

CASE 2 (235663).—Miss T. R., aged eighteen years, was examined, June 20, 1918. She had metrorrhagia and appeared anemic. Her

hemoglobin was 65 per cent and her basal metabolic rate, taken June 22, was −32 per cent.

The hearing tests were normal. Equilibration tests showed a slight spontaneous nystagmus and delayed induced nystagmus; the amplitude also was reduced. The pointing response was of doubtful significance. This case shows mainly a reduction in time and amplitude of nystagmus.

CASE 3 (236779).—Mrs. J. H. P., aged sixty-two years, came for consultation, July 5, 1918. In the course of examination it was found that she had a basal metabolic rate of −32 per cent.

The equilibration tests showed that the stimuli went through, but with reduction in time in nystagmus for horizontal tracts and reduction in amplitude for vertical tracts. Hearing tests showed an eighth nerve reduction, hearing nothing in Schwabach's test. She was given thyroxin in 0.25 mg. doses three times a day and August 1, 1918, her basal metabolic rate was + 1 per cent. Symptomatically she was greatly improved. A Bárány test was attempted. The hearing had improved. In an attempt to test the tracts with cold water she became violently nauseated and the test could not be continued. She had a decided sensation of falling.

This is the only case in the series in which an opportunity was afforded to check up after treatment. The findings indicate that it may be possible in later studies to demonstrate improvement in the results of the Bárány tests.

CASE 4 (262235).—Mrs. W. A. E., aged forty-nine years, was examined, February 28, 1919. She stated that she had noticed an increase in weight, palor, and puffiness, and a change in voice tone. Her skin was dry and her mentality somewhat retarded. General examination was negative, except that the hemoglobin was 10 per cent, and the basal metabolic rate was −22 per cent.

The hearing test showed some reduction in tone appreciation. The equilibration test showed no spontaneous nystagmus and a reduction in amplitude of induced nystagmus, although time reaction was not disturbed. The pointing reaction was not brought out, although there was a slight spontaneous fault with the left.

CASE 5 (262555).—Mr. F. M., aged thirty-nine years, a farmer, came for examination March 4, 1919, complaining of progressive muscular weakness of four years' duration. His skin was yellowish-white. His muscular movements had become markedly slower and he had difficulty in keeping warm. His basal metabolic rate was −40 per cent and his weight was 142.5 pounds.

The equilibration examination showed that in addition to a lowered bone conduction, there was no spontaneous nystagmus. The nystagmus induced with caloric irrigation showed slight delay

and diminished amplitude in the rotatory nystagmus. There was almost no vertigo. The pointing was not brought out with the head erect in the right horizontal canal, but was well elicited with the head thrown back. The left did not respond on the right when the left canal was stimulated, but was present with the left hand.

CASE 6 (270161).—Mrs. W. S., aged forty-five years, was examined, July 7, 1920. She had had a thyroidectomy and her symptoms pointed to insufficient thyroid function. Her basal metabolic rate was —28 per cent.

The equilibration test was negative. The hearing test was normal. The nystagmus time was prompt and the amplitude well marked. There was no past pointing fault, save a failure to respond on stimulation of the left ear, and past pointing with the right hand with the head erect. Other than this discrepancy, it might be said that this patient showed very slight, if any, disturbance as demonstrated by the Bárány test.

CASE 7 (281940).—Mrs. H. M. A., aged fifty-one years, came for examination, August 1, 1919, complaining of general lethargy and decrease in weight. She noticed that she had difficulty in remembering, that mentally she did not grasp things. Her basal metabolic rate was—39 per cent.

Hearing tests were normal, but equilibration tests showed a slight spontaneous nystagmus on looking to right or left and a delayed time in after-nystagmus, with reduction in vertigo. The induced nystagmus was missing in the verticals even after three minutes' irrigation, although the pointing responses were elicited. The horizontal canals gave fair response with the head thrown back. There was no nausea with stimulation. The cerebelli were in normal response, but the reduction was largely in the midstem.

CASE 8 (284646).—Miss L. W., aged fourteen years, came for examination, August 2, 1919, complaining of loss of appetite and weight, and considerable weakness. Her parents had noticed that she was slow of speech and somewhat mentally dull. The examination of the heart, lungs, and kidneys was negative. Her hemoglobin was 74 per cent and her basal metabolic rate was —36 per cent.

The hearing tests were normal. The equilibration tests showed a spontaneous nystagmus horizontal. On irrigation the nystagmus from the vertical tracts was found to be delayed; the after-nystagmus in the horizontal tracts was prompt on the right but not induced on the left. There was also a decrease in the past pointing response from the left with the head thrown back. Otherwise the past pointing was fairly prompt.

CASE 10 (307493).—Miss G. H., aged twenty-six years, was examined, February 27, 1920. She presented rather an indefinite clinical picture, with gradual onset of abdominal distress and some increased nervous instability. Her basal metabolic rate was −22 per cent; her weight was 119.25 pounds.

The equilibration tests showed practically normal hearing. The patient had a slight spontaneous nystagmus but no pointing fault. Under caloric stimulation she showed a delay in responses but no nausea. The pointing reaction was not materially interfered with except the horizontal canal, and it should be noted that the degree of amplitude in the nystagmus induced was less than with the head thrown back. There was no tendency to falling. Irritability was reduced.

CASE 12 (324843).—Mrs. M. F. T., aged sixty-seven years, came for examination, July 16, 1920, complaining of abdominal distention, constipation, shortness of breath, puffiness under the eyes, and swelling of the extremities. The routine examination revealed a basal metabolic rate of −17 per cent, July 23, and − 26 per cent, July 28.

The hearing test was normal and equilibration tests showed no spontaneous disturbance either of nystagmus or pointing. The nystagmus on stimulation was not delayed. There was only slight nausea. The past pointing was elicited well, except on stimulation of the left ear, with the head back, when the left side did not respond, although the right was quite pronounced.

CASE 13 (313335).—Mrs. M. L., aged fifty-seven years, came for examination, April 22, 1920. She had a malignant tumor of the thyroid. Her basal metabolic rate was −25 per cent.

The equilibration test showed slight deafness; no spontaneous nystagmus or pointing fault. On caloric stimulation she was found to have a slight delay in nystagmus time and a slight reduction in past pointing. She was weak and it was doubtful how much the hypothyroidism influenced the tests, or whether the delayed responses might be explained by the patient's weakened condition.

CASE 14 (331963).—Mrs. J. N., aged fifty-three years, was examined, August 30, 1920. The routine tests were made. The basal metabolic rate was −26 per cent.

The hearing test showed only a slight lowering of bone conduction. Equilibration test showed a slight spontaneous nystagmus on looking to the right. On caloric stimulation she was found to have prompt responses of good amplitude. There was good response in the past pointing. Altogether, this case showed very slight changes of indeterminate significance.

TABULATION OF THE CASE HISTORIES

CASE 1 (200923)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	←	→	0	0
Weber's test . .	+	+						
Rinne's test . .	+	+						
Schwabach's test	−2	−2						
C–1	−5	−5						
C–4	−6	−6						

Caloric test—68° F.

Remarks:				
Irritability definitely reduced throughout	1	3	↷ 1′40″	↶ 1′40″
	1	2	→	←

CASE 2 (235663)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent .	Whisper	Whisper	Touch	Touch	←	→	0	0
Weber's test . .	+	+						
Rinne's test . .	+	+						
Schwabach's test	Normal	Normal						
C–1	Normal	Normal						
C–4	Normal	Normal						

Caloric test—68° F.

Remarks:				
Nystagmus very slight, slowly induced; irritability markedly reduced	Touch	Touch	↷ 1′10″	↶ 1′
	1	2		
	1	1		
	Touch	Touch	→	←

CASE 3 (236779)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent .	Loud whisper	Loud whisper	Touch	Touch	0	0	0	0
Weber's test . .	+	+						
Rinne's test . .	+	+						
Schwabach's test	−7	−6						
C–1	−20	−14						
C–4	−15	−10						

Caloric test—68° F.

Remarks:						
Responses retarded	2 2 2 2 Touch	2 2 Touch	↷ 2′10″ ⟶	↶ 1′15″ ⟵		

CASE 4 (262235)

Spontaneous responses.

	Hearing		Pointing.		Nystagmus.			
	Right.	Left	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent .	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test . .	+	+						
Rinne's test . .	+	+						
Schwabach's test	Normal	Normal						
C-1	−10	−6						
C-4	−8	−6						

Caloric test—68° F.

Remarks:						
Time normal; amplitude and responses markedly reduced	Touch 1	Touch 1	↷ 1′35″ ⟶	↶ 1′40″ ⟵		

CASE 5 (262555)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent .	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test . .	..	+						
Rinne's test . .	+	+						
Schwabach's test	−5	−5						
C-1	Normal	Normal						
C-4	Normal	Normal						

Caloric test—68° F.

Remarks:						
Responses delayed, amplitude small	Touch Touch 4	Touch Touch 6 6 8	↷ 1′5″ ⟶	↶ 1′20″ ⟵		

CASE 6 (270161)

Spontaneous responses.

Hearing.			Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test	+	+						
Rinne's test	+	+						
Schwabach's test	Normal	Normal						
C–1	Normal	Normal						
C–4	Normal	Normal						

Caloric test—68° F.

Remarks:						
Responses normal, slightly reduced	4 6 2 4 Touch	4 8 4	↷ 1′	↶ 1′30″		

CASE 7 (281940)

Spontaneous responses.

Hearing.			Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	←	→	0	0
Weber's test	+	+						
Rinne's test	+	+						
Schwabach's test	−4	−3						
C–1	Normal	Normal						
C–4	Normal	Normal						

Caloric test—68° F.

Remarks:						
Rotatory nystagmus not induced	3 14	2 4	0 3′	0 3′		
Rotatory nystagmus not induced	2 ..	3 3 Touch	→	←		

CASE 8 (284646)

Spontaneous responses.

Hearing.			Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent .	Whisper	Whisper	Touch	Touch	⟶	⟵	0	0
Weber's test . .	+	+						
Rinne's test . .	+	+						
Schwabach's test	Normal	Normal						
C-1	Normal	Normal						
C-4	Normal	Normal						

Caloric test—68° F.

Remarks:						
Irritability reduced throughout; no localization	4 4 5 6 1	2 1 Touch	↷ 1′4″ ⟶	↙ 1′30″ 0		

CASE 9 (285377)

Spontaneous responses.

Hearing.			Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent .	Whisper	Whisper	Touch	Touch	⟵	⟶	0	0
Weber's test . .	+	+						
Rinne's test . .	+	+						
Schwabach's test	Normal	Normal						
C-1	Normal	Normal						
C-4	Normal	Normal						

Caloric test—68° F.

Remarks:						
No rotatory nystagmus after three minutes, reduced horizontal; responses reduced	1 1 2 1	3 1 Touch Touch	0 3′ ⟶	0 3′ ⟵		

CASE 10 (307493)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	←	→	0	0
Weber's test	+	+						
Rinne's test	+	+						
Schwabach's test	Normal	Normal						
C–1	Normal	Normal						
C–4	Normal	Normal						

Caloric test—68° F.

Remarks:				
Responses delayed, irritability reduced; no nausea	2	3	↷ 1′26″	↶ 1′32″
	6	4		
	2	3		
	4	4	→	←

CASE 11 (308604)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test	Normal	Normal						
Rinne's test	+	+						
Schwabach's test	−2	−2						
C–1	−2	−2						
C–4	−4	−7						

Caloric test—68° F.

Remarks:				
Responses delayed	1	3	↷ 1′25″	↶ 1′40″
Responses delayed	3	5		
	1	4	→	←
	3	5		

CASE 12 (324843)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test	+	+						
Rinne's test	+	+						
Schwabach's test	Normal	Normal						
C-1	Normal	Normal						
C-4	Normal	Normal						

Caloric test—68° F.

Remarks:						
Time delayed; amplitude small	10	8	↷ 1′	↶ 1′15″		
	10	6				
	10	6	→	←		
	10	Touch				

CASE 13 (313335)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test	..	+						
Rinne's test	+	−						
Schwabach's test	Normal	Normal						
C-1	Normal	−12						
C-4	Normal	−2						

Caloric test—68° F.

Remarks:						
Responses slightly delayed	2	2	↷ 1′10″	↶ 0′50″		
	3	3				
Responses delayed	..	2				
	..	3	→	←		

CASE 14 (331963)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	0	0	0	0
Weber's test	Normal	Normal						
Rinne's test	+	+						
Schwabach's test	−6	−6						
C–1	Normal	Normal						
C–4	Normal	Normal						

Caloric test—68° F.

Remarks:						
Responses fine in character, prompt	6	4	↷ 0′45″	↶ 0′35″		
	4	4				
Responses prompt; slight nausea	5	4	⟶	⟵		
	4	4				

CASE 15 (359522)

Spontaneous responses.

	Hearing.		Pointing.		Nystagmus.			
	Right.	Left.	Right.	Left.	Right.	Left.	Up.	Down.
Noise apparent	Whisper	Whisper	Touch	Touch	⟵	0	0	0
Weber's test	+	+						
Rinne's test	+	+						
Schwabach's test	−2	−2						
C–1	−8	−10						
C–4	−3	−2						

Caloric test—68° F.

Remarks:						
Responses somewhat slow	Touch	Touch				
	9	2	0 3′	↶ 1′45″		
	2	2				
	..	2	⟶	⟵		
	..	3				

On the Bárány sheets it may be noted that retardation in response was demonstrable in 73 per cent of the cases. Cases 1, 2, 7, 8, 9, 10, and 15 show spontaneous nystagmus. Lowered bone conduction* was noted in Cases 5, 7, and 14 only. "Lowered bone conduction" indicates that bone conduction was demonstrated to be lowered in an otherwise normal hearing test, or lowered out of proportion to the rest of the hearing test. There was no spontaneous pointing fault noted.

The caloric test consisted of irrigating the ear with water at 68° F. The nystagmus produced, if any, was recorded; the past pointing test was then made, the head was thrown back, and the nystagmus, if any was noted; the past pointing test was again made. The most prominent finding was that of a delayed response in time or a reduction in amplitude of nystagmus or past pointing, or a combination of all. The degree of retardation was variable, as, for instance, in Case 15, in which nystagmus was absent when the right ear was irrigated and past pointing fault was not noted with the head erect, as compared with Case 6, in which the nystagmus was prompt on the right and responses fairly normal. Case 7 gave no response to stimulation with the head in an erect position with nystagmus, but nevertheless, the stimulus penetrated sufficiently to produce a past pointing fault, with the exception of the left hand and on stimulation of the right ear. In this case, however, with the head thrown back a prompt response was obtained in the nature of a horizontal nystagmus and a well-marked past pointing response. In Cases 1, 2, 3, 8, 10, 11, and 13 there was a generalized retardation or reduction in response to caloric stimulation. In Cases 2, 4, 5, 12, and 14 a reduction in amplitude of the nystagmus and after-nystagmus was found. In Case 3 the responses were retarded, the past pointing test with the right hand and on stimulation of the left ear was not elicited, and the past pointing tests throughout were somewhat reduced. The patient was placed on thyroid therapy and was found within four weeks to have a basal metabolic rate of +1 per cent. She was symptomatically improved, but an attempt to test with the equilibration method was unsuccessful because she was made extremely nauseated and dizzy by the stimulation. In only this one case in the series was it possible to note the effect of the thyroid therapy, but the difference was sufficient to warrant the suggestion that, possibly, thyroid therapy would be beneficial in all of the cases.

In analyzing these cases it was found that the degree of disturbance in the basal metabolic rate in no way indicated the changes that were noted by the Bárány test. The changes are not constant, they are not localized to any one region, and are not of the

* The author published an article on lowered bone conduction test in 1918.

same degree throughout. I believe that the tests demonstrate the fact that myxedema is a condition in which, besides the other changes, there are disturbances of response to stimuli in the eighth nerve tracts which coincide with response to stimuli in other nerve tracts. The exact nature of the pathologic condition causing this disturbance is a matter of conjecture. It may possibly be due to edema of the nerve, to the associated anemia, or it may be a combination of these associated with what may be called a psychical disturbance or high-grade weakness in the higher centers.

Conclusions. 1. In cases of myxedema there is a definite clinical vestibular picture which can be demonstrated by the equilibration tests and is in the nature of a delayed response to stimuli.

2. There is no relationship between the basal metabolic rate and the degree of this retardation.

3. The one case noted suggests the possibility that this clinical picture may be improved by thyroid therapy.

4. These cases are sufficiently interesting to warrant further investigation.

5. The foregoing data may be of very little value in itself, but add materially to the sum total of clinical information.

BIBLIOGRAPHY.

1. Boothby, W. M.: The basal metabolic rate in hyperthyroidism. Jour. Am. Med. Assn., 1921, **67**, 252–255.

2. Denker: Quoted by Lisser.

3. Hammerschlag: Quoted by Lisser.

4. Kendall, E. C.: Isolation of the iodine compound which occurs in the thyroid. Jour. Biol. Chem., 1919, **39**, 125–147.

5. Kendall, E. C. and Osterberg, A. E.: The clinical identification of thyroxin. Jour. Biol. Chem., 1919, **40**, 265–334.

6. Lisser, H.: The eye, ear, nose and throat in diseases of the thyroid and thymus. Ophthal. Rec., 1916, **25**, 433–440.

7. Plummer, H. S.: Interrelationship of function of the thyroid gland and its active agent, thyroxin, in the tissues of the body. Jour. Am. Med. Assn., 1921, **77**, 243–247.

8. St. Lager: Quoted by Lisser.

9. Sajous, C. E. de M.: Internal secretions and principles of medicine. 9 ed. Philadelphia, F. A. Davis Co., 1920, **1**, 188.

10. Sajous, C. E. de M.: The endocrines in otology. Laryngoscope, 1921, **31**, 659–672.

11. Sandiford, Irene: The basal metabolic rate in exophthalmic goiter (1917 cases) with a brief description of the technic used at the Mayo Clinic. Endocrinology 1920, **4**, 71–87.

12. Scholz: Quoted by Lisser.

13. Wagner: Quoted by Lisser.

THE TREATMENT OF THE SYPHILITIC LIVER AND HEART: A THERAPEUTIC PARADOX.

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There is no field of organic disease in which a prognosis under known given conditions is more difficult than in certain forms of visceral syphilis. While syphilitic infection, both acquired and hereditary, affects every viscus, there are two forms of visceral involvement which stand out, by reason of enormous relative frequency, to all others. These are the various forms of hepatic and cardiovascular syphilitic disease. Take away these two great incidents in the sequelæ of constitutional syphilis and the remaining clinical pictures of visceral luetic disease would play a relatively small part in clinical pathology and practice.

It is an accepted fact, and one which makes the whole problem of the diagnosis and treatment of visceral syphilis more difficult, that extensive disease may exist without any clinical manifestations. How common, indeed, is it to find at the post mortem in those dead from old age, accidents or from other causes, the evidence of syphilis in either liver or heart, or both, sufficient, apparently, to have caused marked clinical symptoms from their extensive pathology, unsuspected during life and revealed only at the necropsy. On the other hand how frequent is it to find serious disease with marked symptoms and relatively insignificant changes in the viscera at the post mortem. Prognosis, therefore, cannot be estimated except in a very general way by the apparent extent of damage which is manifest.

Viewing both the syphilitic liver and the syphilitic heart in their various phases as distinct entities, the therapeutic problem connected therewith is made increasingly difficult and more delicate, by the fact that under given like conditions no two cases can be accurately estimated with regard to prognosis.

The tremendous accession to our knowledge of the clinical pathology of syphilis during the last decade may be attributed to three distinct factors: The discovery of the parasite, the employment of the complement-fixation test to diagnosis and the introduction of arsenic compounds as specific therapeutic agents. An enormous awakening of interest in the whole problem of syphilis dates itself from the almost simultaneous appearance in medical practice of these important discoveries. The clinical pathology of syphilitic infection was broadened to include pictures which hitherto were accepted as either possibly being associated with syphilis or in some cases in no way connected with it. In no field of medicine have the boundaries of our knowledge been

extended further than in the newer conception of the syphilitic pathology of the heart and liver.

It is difficult to say that the clinical incidence of syphilitic hepatitis and cardiac disease is more frequent today than before, and their apparent greater occurrence, as well as the manifestations of neurosyphilis, is assuredly explainable upon the basis of more careful examination and the greater inclusion into syphilitic pathology of the various functional and organic diseases of these organs.

It may perhaps be recalled that with the introduction of the original salvarsan preparation, it was distinctly stated in the directions concerning its administration, that cardiac disease and other visceropathies constituted a contraindication to the administration of the drug. Striking results, however, in all forms of syphilis have led to the gradual abandonment of this early precaution, and today it may be stated that the vast majority of syphilitic patients, including those with diseased hearts and livers, at some time or other receive intravenous arsenic medication, in many cases even to the exclusion of other forms of treatment. The great danger, anticipated perhaps by few, of the employment of anything approaching a specific lay in the possibility of the development of a routine or of a "rule-by-thumb" method of treatment. For the most part it may, I believe, be stated that cases now regarded as those of syphilis are treated more or less routinely. Less regard is given the patient as an individual and smaller consideration given to that particular form of the disease which might be predominant in the clinical pathology. To a great extent the dispensary and the hospital, the need of treating a large number of patients in a given time, may be held accountable for the marked tendency to routine rather than individual treatment.

My own experience, I must confess, has not been entirely free from a tendency in this direction, and together with most others it has up to within a short time been my custom to employ, at least some time during the course of the syphilitic's life, one or more courses of intravenous arsenic medication.

It is particularly to the employment of this form of medication in connection with cardiovascular and hepatic syphilis that I would direct attention. I have been impressed, in discussing with older clinicians and in reviewing the literature of pre-salvarsan days, with the fact that either cardiovascular and hepatic syphilis have materially changed in their prognostic outlook, or else they were more intelligently and better treated in pre-salvarsan days than they are today.

The first premise, namely, that the picture has materially changed, is hardly tenable. We are therefore confronted with the second, and it would be well to inquire a little further into the factors and reasons for this. At a day when we know infinitely more concerning the pathology of cardiac syphilis and syphilis of the liver

in their various phases, at a time when we are possessed of improved methods of treatment, it at first may seem strange that our patients have not benefited accordingly.

In regard first to liver syphilis: The incidence of this may be said to be second only in frequency to that of syphilis of the heart. Considering its frequent accidental finding at the postmortem, it is evident that its incidence is far higher than might be deduced from clinical experience.

At the outset it might be stated that great confusion exists in the correlation between the pathologic and the clinical pictures of liver syphilis. The pathologic status of the condition, moreover, is a confused and debatable field among pathologists. It may be accepted that syphilitic hepatitis is due on the one hand to true involvement of the parenchyma, and on the other to primary involvement of the bloodvessels with secondary changes in the parenchyma. Undoubtedly most cases combine both features. In the strictly parenchymatous involvement we may now distinguish early and late forms. The early form is manifested by mild jaundice, transitory and significant only in its possible bearing upon later involvement. The severe form leads to acute yellow atrophy (icterus gravis syphiliticus). Various types of late hepatic syphilis are described as pathologic entities which do not in fact have their clinical analogues. To attempt to differentiate these as clinical pictures leads to inevitable confusion. In the gross and microscopic anatomy of hepatic syphilis certain facts stand out which if recognized and emphasized would lead to a more clear understanding of the clinical phases of the disease.

Late liver syphilis is either diffuse or circumscribed. The diffuse form, consisting of multitudinous infiltrates or miliary gummas, leads to an interstitial fibrosis. The more circumscribed form, consisting of isolated infiltrates and larger gummas, leads spontaneously or under treatment to localized fibrosis. The end-result in either case is identical, a more or less cirrhotic liver. The combination of these two forms is certainly more common than is either one alone.

Reconstructing the pictures clinically, therefore, one may have a small atrophic liver, with or without ascites, and resembling the Laennec type, and a lobulated, either hypertrophic or atrophic liver, cirrhotic only in places, resulting from the circumscribed type. To this latter is given the name "hepar lobatum." The question of the size of the liver depends not so much upon the form of cirrhosis present as upon the time when the patient is seen. Hypertrophy may be seen early, to be followed later by atrophy, either spontaneous or under the influence of treatment. The clinical aspects in a given case depend upon the appearance in one case of tumor, and in the other of obstructive portal circulation leading to ascites, and the combination of these two pictures. There is no reason for a more

detailed description of the various symptoms which may or may not be present with syphilitic cirrhosis. These are familiar to all clinicians of experience.

There are certain mechanical factors present in these cases, however, which are of vital importance in the treatment and which affect the prognosis of a given case. The end-result of all syphilitic processes is a fibrosis. This fibrosis is materially hastened by energetic treatment. The process of repair in a parenchymatous organ in which fibrosis is going on depends upon its ability to recuperate by hypertrophy or by reproduction of its substance. The latter two functions are distinctly slow processes. Treatment, therefore, directed to a diseased organ in which the inevitable and ultimate result, both of the disease and of the treatment, is the production of a scar, should be of the type which leads to a slow rather than a rapid process of repair.

Brilliant results are occasionally achieved in one or the other type of syphilitic hepatitis by energetic and intensive treatment embodying the use of arsenic preparations. This cannot be denied. The consensus of opinion is that, compared with other forms of hepatic disease, syphilitic hepatitis has an admirable prognosis. I wish to concur in this view so far as it applies to the focal types, that is, gummous hepatitis, hepar lobatum and to certain cases of the interstitial type. During the past ten years I have had a very unusual opportunity of studying many cases of hepatic syphilis in its various forms. Given equal conditions I have been struck with the great difference in the prognosis in the various cases of the same apparent type. From the standpoint of prognosis I find myself able to separate the cases broadly into three types: First, syphilitic cirrhosis in which gummous tumors predominate. In a general way the prognosis of this condition stands out as the best of the three types. Second, combined gummous involvement and extensive interstitial hepatitis. In this type as well as in the purely interstitial, non-gummous type an apparent paradox in treatment occurs, particularly when such treatment is intensive. The patients improve with regard to their syphilis and get worse or die of their cirrhosis.

The apparent improvement which one may see in any case of visceral syphilis upon the institution of intensive treatment is not difficult to understand. The predominating clinical feature is but one phase of a widespread constitutional infection. A patient with hepatic syphilis, therefore, may feel decidedly better, his appetite returns, his vascular tone may be better, his color improve, and yet the predominating feature, the hepatic syphilis, may immediately become worse. I believe it may be stated that this is a general experience when the treatment is too intensive and when the process of repair is materially interfered with by the rapidity of connective-tissue replacement. It has been a

common occurrence in my experience for a patient with syphilitic hepatitis to develop his first ascites following the administration of salvarsan. Together with this there may be an intensification of the existing jaundice and a rapid disintegration of the liver, with increasing cachexia of the patient and early death by failure of metabolism. In the same type of case more conservative therapy in the form of mercury and iodide would have resulted in more gradual cicatrization, during which time compensatory hypertrophy might possibly have occurred in various unaffected portions of the organ. Portal obstruction might have been obviated and the patient's ultimate prognosis materially influenced for the better.

Another factor of extreme importance lies in the estimation of liver function. If it were possible by any accurate method to estimate the working capacity of this organ much might be learned with regard to what drug it could best tolerate. We must at this time be convinced of the fact that even to an apparently normal liver the administration of arsenic preparations is not without some danger. Indeed a particular type of jaundice, even in known non-syphilitic cases, can occasionally be produced, undoubtedly by the retention of arsenic in the liver, due possibly to preëxisting disease. With manifest lesions, therefore, in which one can with probability assume a marked degree of dysfunction, it becomes extremely hazardous to employ a substance which in itself may be said to be hepatotoxic, in attempting to alleviate the existing pathology. As an example of the effect of intensive regimé embodying the use of arsenic preparations I beg to submit the brief histories of the following cases, which are typical of those of the class which I am describing and the study of which has led me to the above conclusions.

Case I.—The patient, a man, aged thirty-three years, entered the hospital on June 13, 1919, complaining of swelling of the feet and legs and swelling of the abdomen. The syphilis was contracted fifteen years previously; treatment had been indifferent. One year previous to admission the onset of the disease appeared with a general anasarca. On examination he was found to be markedly emaciated and anemic, slightly jaundiced and to have an ascites and edema of the scrotum. The spleen and liver were both enormously enlarged, firm and hard, with no apparent indentations or nodes on the surface. There was no evidence of cardiac disease, but the lumbar puncture denoted associated cerebrospinal syphilis of the arterial type. In addition he had an old nasal perforation. This patient was given injections of salvarsan, six in number, with a most remarkable improvement in appetite and an improvement in his color and general well-being.

Notwithstanding the fact that he became a bed patient and had

proper diet and rest, his ascites became astonishingly increased. Immediatedly following his last treatment it became necessary to tap him almost every five or six days, and from June 22, 1919, to November 7 over 140,000 cc. of fluid were removed from this patient's abdomen in twenty-six paracenteses. A few weeks before the end of his stay in the hospital he was placed upon the cautious administration of mercury and iodide of potash, with most marked improvement in his ascites, and he was eventually discharged free of fluid in the abdomen. A recent report received from him indicates that he is now entirely well and has resumed his occupation.

His striking improvement in tone, appetite and general well-being can probably be ascribed to the effect of treatment on the syphilis existing outside of his liver. The more serious aspects of his hepatic disease were undoubtedly due to the mechanical causes resulting from a too rapid absorption of syphilitic tissue, its replacement by scar and the rapid shrinkage of the whole organ, associated with the possibility of a toxic effect of the arsenic on the remaining normal liver tissue. His ultimate recovery can without doubt be ascribed to the residual functioning portion of his liver, which fortunately escaped the ensnaring of the new-formed scar as well as the toxicity of the arsenic. I have in mind less fortunate cases, however, in which with far less clinical manifestations the increasing liver dysfunction, accompanied by ever-increasing ascites, led to a fatal issue.

Within the past month I have seen a case in an apparently healthy individual who, following two injections of neoarsphenamin, developed first the onset of apparent acute nephritis. Within two days after the onset coma developed, and this was succeeded by delirium and mania, cyanosis, slight jaundice and death after a stormy course in four days. The only clue to the hepatic pathology of this case lay in slight tenderness and rigidity over the liver region. At the autopsy the picture was that of interstitial hepatitis with beginning acute yellow atrophy and striking syphilitic changes of the heart and aorta.

As illustrative of the effect of salvarsan upon combined syphilitic cirrhosis and tuberculosis the following is cited:

Case II.—The patient, a man, aged forty-two years, entered the hospital on April 11, 1919, complaining of jaundice and loss of weight and weakness. His syphilis dated twenty years previously, at which time he had had indifferent treatment. Two years previous to admission he became slightly jaundiced and began to lose greatly in weight and strength. On examination he was found to have an extremely large liver, very hard and irregular, giving one the impression of linear scarring on its surface. The

spleen was markedly enlarged. The heart was negative to physical examination, but there was an extensive pulmonary tuberculosis demonstrated by physical signs and by frequent sputum examinations. Following very cautious administration of neoarsphenamin, the largest dose being but 3 gm., the patient's abdomen began to fill. Paracentesis yielded about 1000 cc of fluid and was followed by rapid refilling of the abdominal cavity. Following this the patient rapidly deteriorated, became more markedly jaundiced, extremely weakened with rapid loss of weight, and exitus occurred five or six weeks later in stupor, with extreme emaciation and ever increasing anemia. At the postmortem chronic pulmonary tuberculosis, intestinal, mesenteric and peritoneal tuberculosis and miliary tuberculosis in the liver, spleen and pancreas were found. In addition to this he had a typical hepar lobatum, extensive syphilitic cirrhosis and syphilitic myocarditis and aortitis, the latter two not suspected during life. With the combined picture of extensive tuberculosis it is perhaps difficult to say in this case that the outcome would have been different had the treatment been more conservative. I am impressed, however, from a rather large experience with cases in which tuberculosis and syphilis are combined, that neither is markedly benefited by an energetic treatment employing the use of the salvarsan derivatives.

In the absence of laboratory data giving us a clue as to the functional capacity of the normal and diseased liver it seems injudicious to employ in the treatment of any form of syphilitic disease any form of therapy in which the ultimate process of the disease is anticipated, so to speak, by the effect of the treatment. A gradual resorption seems to result in a better functioning organ than follows a rapid absorption and disintegration of the diseased processes. Treatment, therefore, leading to the former would seem to be more desirable and a more rational course to pursue. I believe that salvarsan has no place in the treatment of liver disease. That it can, in certain cases, produce brilliant results, and this must be admitted, is due not to the treatment but rather in spite of it and speaks for the functional reserve of the diseased organ in the particular case. Unfortunately, however, this reserve cannot be estimated. The dictum "Treat intensively and intelligently" in syphilitic disease requires, I believe, modification when the disease presents itself with predominant findings in the liver. The intelligent handling of such a case consists not in the intensive form of treatment but in a more conservative plan, remembering the mechanical processes which might prevent a happy result and with due regard to as yet immeasurable physiologic functioning.

Syphilis, as it affects the heart, has fully as diversified a group

of pathologic pictures as occurs in the liver. As in the latter organ, however, the pictures represent different phases of the same rather than different conditions. Syphilitic myocarditis, for example, viewed pathologically, may be the result of diffuse interstitial infiltration, the disintegration and absorption of multiple minute gummas, degenerative changes near the terminals of the coronary arterioles, and muscle degeneration and replacement following obstruction or obliteration of the minute coronary vessels (myelomalacia).

Clinically, however, these varied pathologic processes present themselves as more or less severe grades of myocardial disease. Quite apart from these are the various pathologic findings in and about the base of the aorta and the aortic ring as well as those on the aortic flaps, giving the clinical picture of varying degrees of aortitis and aortic regurgitation. Coronary involvement, a still third pathologic and clinical picture, is probably so universally associated with myocardial disease that its clinical syndrome may be regarded in the symptom-complex of myocarditis. Endocardial changes involving the other valve cusps have been described, but are of such rare occurrence that, viewed from the standpoint of frequency, they may be disregarded here. As Harlow Brooks has properly pointed out, the regular, almost universal association of myocardial disease with aortic aneurysm in any form, and aortitis, brings these two conditions into a prominent place in the consideration of cardiac syphilis. Broadly speaking, therefore, clinical syphilis of the heart resolves itself into a consideration of the symptoms dependent upon myocarditis, arotic regurgitation, aortic aneurysm, syphilitic aortitis and coronary disease. It is highly probably that none of these conditions exists alone. Disease of the heart muscle may be said to be almost concomitant sooner or later with all of the aforementioned. As Brooks and others have properly brought out, the treatment, of the syphilitic heart resolves itself into two distinct factors; the syphilitic infection on the one hand and the cardiac defect on the other. These two completely distinct problems suggest at once that the proper management of such cases necessitates a knowledge on the one hand of the physiologic pathology of the heart and its treatment and on the other hand a broad comprehensive knowledge of the systemic disease. Herein, I believe, lies the explanation of the fact that today medical men are not as well equipped for, nor are giving as intelligent treatment to such cases as were their predecessors of two or three decades ago. Today not only has the periphery of our knowledge concerning syphilis been tremendously extended, necessitating the development of specially trained men in this disease, but the field of internal medicine has reached far into the realm of biochemistry and physiologic pathology. The inevitable result has been that the syphilologist, highly specialized but

lacking modern diagnostic methods of cardiac disease, treats the cases from the standpoint of the general infection, and too little attention is paid to the predominating dysfunction, namely, the diseased heart. Viewed from the other side, the internist, fully equipped with modern methods of cardiac investigation, naturally finds his chief interest in the predominating feature, namely, the diseased heart, and the extensive associated constitutional features of the case are oftentimes slighted in its treatment.

Surely a happy medium suggests itself for the correction of this natural tendency to error. The cases should be studied and treated from the standpoint, first, of the disease, and secondly, from the cardiac defect. In hospitals the ideal can be achieved when the case can have the benefit of the combined efforts of those properly equipped.

It is entirely apart from my purpose, and I am unequipped by training, to discuss the treatment of the cardiac defect in a given case.

From a rather extensive experience, however, in the management of such cases as have been described above, in collaboration with those admirably equipped to treat the cardiac defect, I have reached some very definite conclusions as to what constitutes the intelligent treatment of cases of cardiac syphilis.

My experience with salvarsan in these cases dates almost from the time of the introduction of the drug, notwithstanding the instructions which were sent out with the early packages, that cardiac disease constituted a contraindication. As I stated before I believe this fundamental error is largely practised, and few cases of syphilis are, indeed, denied at some time during their course the benefits which might be derived from the intravenous administration of salvarsan. Indeed so universal has this become that patients actually demand that form of treatment and view with suspicion any tendency to withhold it from them.

Even with due regard to the warnings concerning the contraindication of the drug, many cases of unsuspected non-symptomatic cardiac syphilis receive salvarsan; notably as is true of the very early cases of myocarditis in which the symptoms only become manifest after the treatment. It must be recalled at this point that actual cardiac syphilis in the very early months of the infection, coincident, indeed, with the exanthem, may be present either without any symptoms or with such slight clinical findings as arrhythmia and tachycardia. This last group of cases, however, probably does not present the serious problem that the later ones, in which the cardiac defect is the predominating feature of the case do, and brilliant results perhaps may be achieved in these cases with the intensive form of treatment. I have in mind, however, one case in which such treatment resulted in heart-block and in a marked accentuation of early suggestive features, so that

well-developed myocardial disease resulted in the first year of the infection.

In the early forms of myocardial disease also, and in many cases of aortic regurgitation, both compensated and decompensated, I have seen extraordinarily happy results from the use of the intensive administration of intravenous arsenic medication. As in syphilis of the liver, however, it is impossible to say in a given group of cases just exactly how an individual may react. Thus it has been my unfortunate but instructive experience to note in cases in which a happy result might be expected, intravenous medication has resulted in decompensation or acute dilatation and failure in the myocardial and aortic groups. Two cases of aneurysm in my experience have ruptured, and numerous cases of aortitis and of coronary disease have become unfortunately worse in regard to the cardiac aspect of their condition.

It is not difficult, I think, to find the source of the explanation for these unfortunate accidents. Taking the group of myocardial cases and discussing them now solely from the standpoint of syphilis, I have been impressed with the fact that these hearts untreated are frequently better functioning organs than when subjected to violent intensive therapy. There is at least some reason for believing that mechanical causes may explain this. The syphilitic infiltrates, particularly in the more diffuse form, while they unquestionably materially weaken muscle tone and function, have, as is well known, a certain degree of elasticity. Their rapid replacement or disintegration may lead to actual gaps and to such a rapid fibrosis that many otherwise normal heart-muscle cells disintegrate or are snared off in the cicatrizing process, and the result is further embarrassment, most often manifested by acute dilatation. Compensatory hypertrophy is, perhaps, nowhere seen so admirably as in the heart muscle. A compensatory hypertrophy, however, requires time, and means the slow absorbtion of diseased process and the slow recuperation of non-diseased muscle fibers. This, I believe, can be achieved, and is when the syphilitic heart is treated from the standpoint of its syphilis, at least slowly, and due attention is paid to it from the side of the defect. Not only may it be stated that the intensive treatment of the syphilitic heart is injudicious because of mechanical reasons, but such treatment is, indeed, at entire variance with what might properly be regarded as the effort to keep and enhance a cardiac reserve, which is the aim of the treatment directed to the defect alone. Another factor, at least of some possible bearing in producing acute failure, is the introduction into the blood stream of a not inconsiderable amount of fluid. This applies, of course, to preparations of the so-called "old salvarsan" derivatives, which necessitate the introduction of 100 cc or more of fluid.

It has been possible for me, in individual cases in which for

other reasons I have withheld salvarsan and its derivatives and employed more conservative forms of treatment, as well as in groups of cases in which I intentionally withheld the drug, to compare such groups with those treated more intensively. In both types of cases I have had the benefit of expert advice on the part of my associates in internal medicine who have treated the cases with me from the standpoint of the cardiac defect. In not a single case that I can recall of either aortitis, myocarditis or aneurysmal disease can it be stated that any untoward accident happened immediately following the institution of the treatment. In fact the reverse may be said to have been the general rule. Improvement, slow to be sure, almost invariably took place. On the other hand it must be stated that the improvement in the patient's general condition was not so striking in cases treated more conservatively, for example, with mercury and iodide. It has been a not infrequent occurrence for patients treated intensively to have an immediate betterment of their general condition, a better color and a feeling of general well-being. This, in every case, I believe, is due to the effect of the treatment upon foci elsewhere, which have been dispersed, and to a general effect upon the circulation. Such a change is not so apt to occur when iodide and mercury are given—at least the change, if it does occur, is usually later, and particularly after the drugs have been withdrawn.

The remarkable improvement in general following the arsenic treatment has often been followed in some cases by a most rapid deterioration, with evidences of accentuation of the original cardiac defect. Here one can only surmise at two possible explanations, both of which are probably factors: First, that the syphilitic products have been too rapidly replaced by scar tissue, or, second, that their rapid disintegration has produced a chemical change deleterious in its effect on the local lesion.

Here, therefore, as in liver syphilis, we are confronted with the remarkable paradox that the patient gets well or better of his syphilis, and may die as the result of the dispersion of his syphilitic cardiac lesion.

I should like briefly to summarize a few cases illustrative of the above conditions:

Case I.—*Syphilitic Aortitis.* The patient, a man, aged forty-four years, entered the hospital on March 23, 1920, having been transferred from the department of medicine with a diagnosis of syphilitic aortitis. He denied knowledge of syphilis. His present trouble manifested itself as shortness of breath two years previous to admission. This became more marked until, on admission, he could not lie down for more than an hour at a time, nor could he give himself the slightest exertion without developing a marked

dyspnea. In addition he had considerable palpitation and some precordial pain. The clinical findings were those of aortitis and typical regurgitation. The patient received two injections of small doses of neoarsphenamin, only 2 gm. to which he immediately reacted with marked improvement. His symptoms and pains disappeared, his dyspnea, while present, was markedly less, and in a short time he was dismissed from the hospital for observation. Within a very brief time the patient returned completely decompensated, and it was only with the greatest difficulty that his reserve was brought up to such a point that he could again leave the hospital. His second respite was even shorter, and he has returned twice since, both of which times he was in so desperate a condition that it was believed he could not recover. At the present writing he is still living but without any reserve, and practically bedfast.

CASE II.—*Tabes Dorsalis, Aortitis, Aneurysm of the Arch, Both Unsuspected.* The patient, aged forty-six years, entered the hospital for treatment for syphilis. His infection dated back some twenty-four years, at which time he had had indifferent treatment. His present trouble began four years ago with failure of eyesight and pains. On examination he was found to have a typical tabes dorsalis, with all the classical findings. This patient received but two injections of arsphenamin, 3 gm. and four and five-tenths respectively. The second injection was followed by severe headache and attacks of dizziness as well as numbness and cold sweat. He became very cyanotic and within a few days was bedfast. At this time the first suggestion of a cardiac defect manifested itself in marked arrhythmia, weakness of the pulse, general asthenia and cyanosis and signs of cardiac dilatation. He continued in this condition for about three weeks and died suddenly in bed during the night. At the post mortem he was found to have aortitis, aneurysm, myocarditis and syphilis of the cord and brain.

This case I believe to be extremely interesting and valuable, as showing the regular association of cardiovascular and other forms of visceral syphilis, with the predominant findings those referring to the nervous system. I have seen frequent examples of this, and their occasional occurrence has made me more cautious in the use of intensive intravenous medication in cases of neurosyphilis until I have been completely satisfied and have been assured by my internist colleagues that such patients are free, or apparently so, from evident cardiovascular disease.

CASE III.—*Syphilitic Aortitis and Myocarditis.* The patient, aged forty-four years, entered the hospital, having been referred by the department of internal medicine with a diagnosis of old syphilis and aortitis. His infection dated twelve years previous

to his admission, and treatment had at that time been indifferent. Two years previous to admission he noticed shortness of breath, weakness, dizziness and difficulty in walking. These symptoms were accompanied by sharp pains in the right side of his chest. The clinical findings were those of aortitis and regurgitation, well compensated, otherwise negative. This patient received seven injections of neoarsphenamin, the largest being only 3 gm. and the smallest. 1+. These injections were decidedly small, as I had begun to feel when he was treated that maximum dosage must be avoided in these cases. Following his injections the patient developed typical attacks of angina pectoris, these occurring very frequently. They were associated with cyanosis, collapse and syncope, so that it was feared that he might die any time during the attack. During the patient's stay in the hospital, some eight weeks, he was completely bedfast. Only after all medication had ceased and the strictest attention was paid to the cardiac defect as such did he show any sign of improvement. Under iodine and mercury, which were administered during the latter part of his stay, he gradually improved, so that the attacks finally completely ceased, his dyspnea disappeared and he was able to be discharged from the hospital.

These cases are but a few of many which I have seen, both in the hospital and private practice, in which the result, frequently fatal, more often deleterious, could justifiably, I think, be ascribed to the type of the treatment employed.

I am a most ardent advocate of the use of arsphenamin in the treatment of syphilis. However, notwithstanding the fact that brilliant results may sometimes be achieved in cases of severe visceral disease, I am of the opinion that it should not be used as a routine measure in the treatment of cardiac and hepatic syphilis. When indicated in these two conditions it may be used with reasonable safety in those cases which have responded to a previous administration of mercury and iodide. The great difficulty and the necessity for taking a positive stand lies, I believe, in our inability to properly estimate the new case from the standpoint of prognosis when it is first seen. With everything in its favor apparently, from the extent of the lesion, the shortness of its duration and the general well-being of the patient, a case of cardiovascular or hepatic syphilis may well turn out to be one with serious or even fatal sequelæ. The converse, of course, must be admitted, that cases with the most serious aspects from the standpoint of the extent of lesions and general condition of the patient may react favorably to intensive treatment.

In mercury and iodide we have two drugs admirably suited for the treatment of cardiovascular and hepatic as well as other forms of visceral syphilis. Their action is slow, and this, I believe,

is desirable. In all cases their use should be combined with the intelligent treatment of the diseased heart, and this can only be done in collaboration with the internist. On his part the internist may find useful in the management of such cases the very special knowledge which the syphilologist has of the various salts of mercury, their different uses in different types of individuals, the advantage of frequent change and more particularly the management of the constitutional side of the infection.

In the employment of newer and more potent arsenic preparations, which are constantly being introduced, I believe it is safe to predict that even greater disaster and more frequent fatality may occur when these drugs are used in the treatment of the visceral forms of the disease. The syphilized liver and heart, in whatever stage of the disease, from clinical experience at least, seem to do better when the process of repair is slow and when no great strain is placed upon their normal functioning activities.

ACUTE LUNG ABSCESS TREATED BY THERAPEUTIC PNEUMOTHORAX.

By Herbert M. Rich, M.D.,
DETROIT.

The danger and the high mortality of surgical drainage of pulmonary abscess lend importance to the discussion of any method which will improve our results in these cases. It has seemed worth while, therefore, to report the following experiences with the hope that as case-records accumulate we shall be able to steer a safe course in the treatment of acute pulmonary abscess. The cases here reported are all non-tuberculous.

Nomenclature. The term lung abscess is a somewhat ill-defined expression for intrapulmonary pus. It may be diffuse or circumscribed, acute or chronic, gangrenous or not. It is frequently an extension from a purulent process in the neighboring tissues, as empyema, lateral or interlobar. Its etiology has many items. For the purpose of this paper, pus in the lung, the result of burrowing from an interlobar empyema, ultimately reaching a bronchus, is called a lung abscess. There seems to be no single pathologic term in English which will describe this condition. Other processes producing free pus in the lung are included under this term, the etiologic items being mentioned in the separate case reports. This explanatory paragraph is inserted because of the lack of satisfactory nomenclature for these conditions, causing confusion in the mind of the reader.

CASE REPORTS. CASE I.—Miss B., stenographer, aged twenty-one years. Bronchopneumonia. Lung abscess. Pneumothorax successful. Recovery.

First seen October 16, 1919. Had been ill with bronchopneumonia six weeks; fever, chills, pain in right chest until it "broke." For one week there had been daily evacuation up to one pint of pus, extremely foul smelling. Temperature, range 101° to 104° F. Great prostration and weakness. Physical findings showed impaired resonance over the lower lobe right lung, surrounded by zone of moist rales of great variety. No signs of fluid or tuberculosis. Diagnosis of lung abscess or interlobar empyema was made and compression of the lung by means of therapeutic pneumothorax advised.

Entered Harper Hospital, Detroit, October 21. Temperature, 102° to 104° F. Weight, 84 pounds (usual weight, 96 pounds).

October 24. Pneumothorax attempted in fifth interspace of the right axilla. Pleura very thick; strong pleural reflex with severe pain; 50 cc sterile air injected, but was obliged to discontinue because of spasm of diaphragm due to pleural reflex.

October 25. Pneumothorax in third interspace; 300 cc air introduced. Followed by only slight pain, but in a few hours by greatly increased cough and expectoration. Seemed much better two days later, but foul sputum continued in small quantity.

October 30. 250 cc of sterile air.

November 6. 300 cc of sterile air followed by some pain at the base of the right lung. Cough and expectoration disappeared.

November 9. Patient left hospital apparently well. Weight, 90 pounds. Sputum repeatedly negative for tubercle bacilli. Frequent reports from the patient since up to June, 1921: Has remained in good health and without cough or expectoration.

CASE II.—A. S., lawyer, aged forty-eight years. Simple cold followed by lung abscess. Successful pneumothorax. Recovery.

Never ill in bed since infancy.

October 23. Had cold. October 25. Went to Oklahoma. Had fever, chills, bad cough, sputum became purulent about November 2. First seen November 6. Temperature, 100.8° F. Paroxysmal cough, odor of sputum extremely foul. Physical examination showed an impaired resonance and bronchial breathing in the right axilla, at 4th and 5th ribs, surrounded by a zone of coarse and fine moist rales. Sputum negative for tubercle bacilli.

Entered Harper Hospital November 12. Temperature, 101° F. Roentgen ray. "Fluoroscopic examination: Chest in erect position shows abscess described previously in the right upper lobe. There is definite evidence of cavity formation. The right upper lobe is apparently immobile. Free excursion of diaphragm on both sides." (Allison)

Pneumothorax, anterior axillary line, in 4th interspace; 275 cc of sterile air introduced.

About twenty-four hours later the patient had a severe paroxysm of coughing, with evacuation of a large quantity of sputum and alarming exhaustion. This was the last of the severe paroxysms of cough.

November 14. Pneumothorax attempted. Slight pleural shock from the needle used in giving local anesthetic. No gas given.

Patient continues to improve. Temperature not above normal after November 19. Left hospital November 28. Entirely free from symptoms; last seen June, 1921.

This was a case of interlobar empyema, opening into a bronchus, following a simple cold. Nothing else so far as I know can answer the roentgen-ray description of a cavity partly filled with fluid, later disappearing entirely. Evacuation was induced by very slight compression and recovery was prompt and satisfactory.

CASE III.—Miss K., aged nineteen years. Appendectomy with drainage. Influenza. Bilateral bronchopneumonia. Lung abscess. Pneumothorax successful. Death.

Never ill in bed until January 10, 1920. Acute suppurative appendicitis; operated in local hospital; drainage established.

January 25. Said to have had influenza followed by double bronchopneumonia. Temperature normal in ten days, then chill, fever, pain in region at base of right lung. First seen February 22. Temperature, 104° F. Patient emaciated, pale, panting, anxious, very weak, pulse 140. Open wound in abdomen with foul discharge. Exhausting paroxysmal cough, raising at intervals 4 to 6 ounces of sputum, extremely foul odor. Examination of chest: Relative dulness in irregular area of lower right lung. Many coarse, moist, bubbling rales. No evidence of fluid.

Entered Harper Hospital, February 24. Temperature, 101.4° F. Pulse, 132. Symptoms and signs unchanged. Sputum, negative for tubercle bacilli; pneumococcus, Type IV.

March 1. Symptoms continued without improvement, so compression was undertaken as a last resort. Pneumothorax needle introduced in 4th intercostal space of right anterior axillary line. Pleura thickened; no oscillation; in third intercostal space, good oscillation and 350 cc of sterile air introduced. Later, coughed up several ounces of foul sputum. Felt relieved and coughed much less until death the following day from asthenia. No autopsy permitted.

It is obvious that the fatality in this case was not due entirely to the lung abscess nor to the pneumothorax.

CASE IV.—Mrs. T., aged thirty-one years; pregnant five months; influenza. Interlobar empyema; evacuation into bronchus; successful pneumothorax; recovery.

Seen February 16, with recurrent paroxysmal cough and great expectoration of five weeks' duration following influenza; pregnant five months; paroxysm very severe, leaving patient exhausted, limp and expecting to die. Previous history unimportant. Signs of abscess in lower lobe right lung.

Entered Harper Hospital February 16. Temperature, 103° F. Pulse, 120. Urine negative. Sputum negative for tubercle bacilli. Pneumococcus, Type IV. Blood: 16,000 white cells, polynuclears, 52 per cent. Patient did not improve.

February 18. Pneumothorax needle inserted in midaxillary line, 4th intercostal space. Gave 550 cc of sterile air. Very severe paroxysm of coughing about six hours after first injection of air. Emptied out a pint of purulent fluid. Much relieved. Temperature reached normal four days later. Never had severe cough after that day. Second injection in seven days, February 25. Left hospital March 3, free from symptoms.

June, 1921, reported quite well by family physician, never having had any return of symptoms.

In this case the pathology was probably an interlobar empyema burrowing into the lung.

CASE V.—Mrs. P., aged thirty-one years. Influenza; pneumonia; lung abscess in upper lobe. Spontanious recovery.

Two children. Never ill since childhood until influenza in January, 1920. Pneumonia followed. First seen three weeks later, February 10. Terrific paroxysms of coughing with large quantities of fluid, offensive pus. Signs of interlobar empyema, probably between upper and middle lobes on right.

No roentgen-ray taken then. Patient reluctant to go to hospital and a few days later began to improve and ultimately recovered. Roentgen-ray six weeks later showed most of lung clear, the only sings of the recent trouble being increased linear markings in the right lung.

June, 1920. In good health.

This was an instance of so-called spontaneous recovery.

CASE VI.—Miss D., aged twenty-nine years. Similar to Case V. Social worker, never ill before. Seen February 15, 1920. Paroxysmal cough, bringing up at times more than a teacupful of purulent sputum. Sputum had pinkish tint. Temperature, 102.8° F. Profuse sweats. Profound exhaustion. Refused hospital. Gradual improvement. Left city several weeks later, in good condition.

Another spontaneous recovery.

CASE VII.—A. F. aged forty-two years. Mechanic. Bronchopneumonia followed by lung abscess. Successful pneumothorax. Recovery.

Entered Harper Hospital, service of Dr. Freund, April 4, 1920. Complaint—fever, cough with blood-tinged sputum, dyspnea, weakness. Previous history negative. His symptoms have been gradually developing for ten days. Physical examination showed extensive pyorrhea and many crowned teeth which later proved to cover five dental abscesses, one very large. There was dulness over the upper half of the right chest and in the upper axilla. Whispered voice increased over a part of this area. Breath sounds were variable, distant in some areas with bronchovesicular predominant. Fine and coarse rales. Temperature range, 101° to 103° F. Wassermann negative. Temperature down to normal on sixth day with 101° F. in evening. Continued to have 99° to 103° F. daily. Sputum negative for tubercle bacilli; pneumococcus, Type IV. Symptoms continuing and patient becoming weaker. On May 20, therapeutic pneumothorax was induced. Puncture in 8th intercostal space below point of scapula. 550 cc of sterile air given.

May 23, 200 cc of sterile air were given. Patient improved promptly. Temperature approached normal; cough and expectoration less; appetite and strength improved.

May 29. Roentgen ray report: "Outer fourth of upper right lung filled with an area of density, extending toward the midlung field opposite to the third interspace. There is evidence of a partial collapse of the lung, the extra density is probably due to thickening of the pleura." W. A. Evans.

June 3. 200 cc of sterile air injected.

June 12. Patient discharged from hospital, apparently well. Seen on August 1 and had continued to that time without symptoms. Had gained 42 pounds.

The sequence in this case was undoubtedly first multiple dental abscesses; second, lobar pneumonia; third, lung abscess.

Case VIII.—Mrs. C., aged twenty-eight years; pregnant seven months. Influenza. Lung abscess. Compression successful. Recovery.

February, 1920. Influenza, followed by lung abscess in left lower back. First seen March 12. Had been ill six weeks. Daily evacuation of twelve to fifteen ounces of foul pus; very weak; no fever. Also pregnant and fearing miscarriage from cough. Usual signs of abscess. Had had three "dry" punctures. Pneumothorax with 500 cc of air injected on March 13. By March 17 the twenty-four hour amount of sputum was reduced to five ounces. On March 18 there was none. Practically no cough after this. Patient left hospital on March 21, and resumed household duties.

March 30, 500 cc of air given. Has remained well since and been successfully confined.

CASE IX.—Mrs. P., aged thirty years; operation on cervix; lung abscess; unsuccessful attempt at pneumothorax; surgical drainage; death.

Had two children. Never ill. Was operated for laceration of cervix, leaving hospital July 24, 1920, convalescent. One week later pain in lower right chest; sudden onset. Respiration painful. Temperature, 103°F. Marked dyspnea. After continued fever for six days the temperature dropped and a pint of blood-stained, foul-smelling purulent sputum was expectorated. Two days later fever again appeared and septic temperature continued until first seen with Dr. George E. McKean, August 26. At this time she had physical signs of an abscess of lung under right breast. Roentgen-ray showed a fluid level, the lateral oblique plate showing that the abscess anteriorly was very near the external pleura.

August 28. Therapeutic pneumothorax in the fourth intercostal space, midaxillary line, 500 cc of sterile air injected. Pleura distinctly thickened. Violent coughing following with considerable subcutaneous emphysema. During the following twenty-four hours the abscess perforated into the pleural cavity under the right breast. The condition was then complicated by this pyopneumothorax, which was operated under local anesthesia by Dr. Max Ballin, August 29. Ample drainage was established, but the patient did not rally and died August 31 from pulmonary edema.

In this case there was a septic embolus from the cervix. The abscess was near the periphery of the lung. To attempt pneumothorax in such a case is undoubtedly a mistake.

CASE X.—Mrs. B., aged twenty-five years. Tonsillectomy; lung abscess for five months. Pneumothorax successful. Recovery.

Tonsillectomy in December, 1916. Four days later had pneumonia, lasting two weeks. Shortly after began expectoration of foul-smelling, purulent sputum. Had cough, pain, sputum, occasionally bloodstreaked. Coughed more on first rising in morning; also when lying on right side. This continued all winter. Was slightly better in summer, but symptoms reappeared in the fall, 1917. Went to California, January to March, 1918. Seen first after return. Temperature, 100.6°; pulse 120, sitting; weight, 203 pounds. Complaint, pain in right upper thorax; night-sweats, cough and foul sputum continue.

May 27, 1918, therapeutic pneumothorax induced by 300 cc of nitrogen in the right pleural cavity. Was followed by severe pain for one day. No increase in amount of sputum.

June 4. 550 cc of sterile air. Had considerable pain and some subcutaneous emphysema.

June 20. No fever, cough or foul sputum since last injection.

Gave 400 cc of sterile air. Had pain in back and neck for one day. No more night-sweats.

This was the last treatment. Symptoms disappeared and there has been no reappearance up to December, 1920.

This abscess could hardly be called acute, and compression was obviously imperfect, owing to adhesions. It shows that the pneumothorax method may be useful even in the presence of adhesions, and that complete collapse of the lung is not necessary in every case.

Spontaneous Cure. It should be pointed out that a certain number of cases of pulmonary abscess empty out through a bronchus and recover perfectly. I have seen 3 such cases, and the medical profession of nearly every community has traditions of such happy cures. In 1 case, which I studied three years after such spontaneous evacuation, neither physical examination nor roentgen ray revealed any evidence of permanent change in the lung. This abscess followed a tonsillectomy and had been active four weeks. The spontaneous evacuation occurred one hour before the operation for surgical drainage was to be done.

In the 3 cases of spontaneous cure here noted the abscess in each case was in an upper lobe. It seems certain that spontaneous cure is much less likely to occur when the lesion is in a lower lobe. While these do often discharge into a bronchus, their evacuation is usually only partial and the coughing necessary is so severe and exhausting as to be highly alarming. The inverted posture assists the cough in emptying the contents of the abscess, but in the event of a tortuous fistulous track does not help greatly. In the present series of cases inversion of the person was only occasionally useful.

It would seem then that while upper lobe abscesses may be spontaneously cured it is highly improbable that those in the lower lobe will. It is extremely important that one should not be misled in prognosis by the fact that a lower lobe abscess is discharging pus through a bronchus. This does not mean that efficient drainage is established, and while waiting for spontaneous cure one may allow the time to pass in which the lung could be successfully compressed and a perfect cure effected.

Time for Operation. In this series the oldest abscess successfully treated was of eight weeks' standing with the exception of Case X.

In Tewksbury's series of 10 acute cases the latest successful one was of six weeks duration. The most advantageous time would seem to be between the second and fourth weeks. The development of adhesions to the outer chest wall will depend largely on the position of the abscess. When near the periphery, adhesions will quickly form and perforation into the external pleural cavity is the event to be expected. It is doubtful if compression should

be undertaken in these cases. On the other hand abscesses near the hilus, where most difficult to reach for surgical drainage and where bronchial fistulæ are most likely to persist, are easily and promptly cured by a mild compression. Since the therapeutic pneumothorax is painless and harmless the question arises whether one is ever justified in carrying expectant treatment more than two weeks.

One factor which must be insisted upon is the continuance of the treatment until the lesion has had time to heal. While a short compression may be followed by the most happy results, one should maintain the compression for four weeks in acute cases and much longer in chronic cases. Such chronic cases, however, may safely leave the hospital in a few days, doing light work and merely returning at regular intervals for refills.

Etiology. Of the 10 cases here cited:

One followed a pelvic operation, the colon bacillus predominating in the lung abscess, undoubtedly a septic infarct.

One followed a simple cold.

One followed tonsillectomy under ether anesthesia.

Two followed bronchopneumonia.

Four followed the influenza-bronchopneumonia syndrome. In several of these cases the roentgen-ray findings made it certain that interlobar empyema preceded the abscess formation.

Eight of the 10 cases were women; 2 men. All were adults twenty-one to forty-eight years. None of these gave a history of previous lung disease. In fact, in none of these patients was there any history of previous severe illness of any character. Repeated examinations for tubercle bacilli were made in every case, and all were negative.

The time of development varied greatly. In Case II, a simple cold developed fetid sputum in five days. Two cases of bronchopneumonia "broke" in about six weeks. The lung infarct following operation on the cervix, developed two weeks after operation (Case IX). In none of the influenza cases could the time be accurately fixed. In each of these symptoms ultimately showing abscess developed about three weeks after the onset of the pneumonia.

Prognosis. Under the older methods of treatment the outlook for a case of pulmonary abscess is indeed discouraging. Spontaneous recovery is very uncertain and is not due to any treatment. Forchheimer quotes the figures on 133 cases with less than 10 per cent recovery and death in 64 per cent. Other figures are more favorable for small numbers of cases. However, the surgical treatment involves a highly difficult and dangerous operation, and Lord makes the statement that "incomplete cure is the rule." Combining the cases reported by Tewksbury with those here detailed, there are 20 cases of acute abscess with 16 instances of prompt and complete recovery, or 80 per cent.

Comment. The literature on this form of treatment in abscess is limited. The procedure was first proposed by Forlanini, and later, 1910, he reported a case of chronic lung abscess of six years' duration following croupous pneumonia. Treatment was continued twenty-five months with great amelioration of symptoms. He does not record the treatment of any cases of acute abscess, but Schmidt, in 1908, in reporting experience with pneumothorax in a variety of conditions, mentions its use in three cases as follows:

1. "Aspiration-pneumonia," six months' duration. One injection of 1000 cc of sterile air. Much better in two weeks; discharged from hospital cured in four weeks.

2. "Fetid bronchitis," several years' standing, worse last few few weeks. No response to previous treatment. Tubercle bacilli present in sputum. Prompt improvement under treatment, which consisted of one injection of 300 cc of sterile salt solution. Patient gained eighteen pounds in five weeks. Discharged cured. Seen two years later with no return of symptoms.

3. "Fetid bronchitis," with induration in right lower lobe. Had been ill without improvement from September to February (five months). One injection of 1200 cc of sterile air. Patient left hospital in one month, apparently well, seen thirteen months later, no recurrence.

Whether these cases should be classed as bronchiectasis or lung abscess is difficult to say. The report of cure by a single injection, one by the use of salt solution, is at least interesting and stimulating.

Tewksbury in two papers reports in all 10 acute cases with 8 recoveries and 2 deaths. In the fatal cases the compression was not directly connected with the cause of death, as both cases had serious disease aside from the lung abscess.

Summary.—Ten cases of pulmonary abscess are reported. Eight were treated with therapeutic pneumothorax. There were 8 complete recoveries and two deaths—two spontaneous recoveries.

The experiences here related corroborate those of Tewksbury in every particular. Acute pulmonary abscess may be promptly and completely cured by therapeutic pneumothorax. A possible exception should be made in those cases where the abscess is located near the periphery of the lung.

REFERENCES.

1. Tewksbury, W. D.: Jour. Am. Med. Assn., March 10, 1917.
2. Tewksbury, W. D.: Jour. Am. Med. Assn., February 2, 1918.
3. Simon and Swezey: Am. Rev. Tuberc., 1918.
4. Schmidt, A.: Beit. zur. Klinik der Tub., 1908, Bd. **9**.
5. Forlanini: München. med. Wchnschr., January 18, 1910.

REVIEWS.

ORAL ROENTGENOLOGY. By KURT H. THOMA, D.M.D., Assistant Professor of Oral Histology and Pathology, and Member of the Research Committee, Harvard University Dental School; Oral Surgeon, Robert Breck Brigham Hospital, etc. Second edition, revised and enlarged. Pp. 341; 470 illustrations. Philadelphia and New York; Lea & Febiger, 1922.

IN the second edition the author has added a description of some of the roentgen-ray machines and tubes now in use for dental work, and has also outlined the principal features of the technic of making intraoral and extraoral films of the teeth and alveolar processes. A little more space given to the dangers of overexposure to the roentgen rays and of high-tension electric currents would have been helpful, especially to beginners.

The bulk of the work is devoted to interpretation, and the numerous illustrations depict very beautifully almost every conceivable abnormality of the hard tissues of the mouth and jaws. Normal roentgenographic studies are shown for comparison. It is particularly emphasized that diagnosis should not depend on the roentgen-ray examination alone; the latter gives evidence, which should be correlated with the history, physical findings, tests and laboratory findings.

The book is to be regarded as a highly reliable source of information to both medical and dental practitioners. It is particularly welcome in view of the almost universal employment of the roentgen ray by dentists, many of the latter having had no training in its use other than that imparted by the dealers. R. H. I.

TUBERCULOSIS AND THE COMMUNITY. By JOHN B. HAWES, 2d, M.D., Director of Clinic for Pulmonary Diseases, and Assistant Visiting Physician, Massachusetts General Hospital, etc. Pp. 168. Philadelphia: Lea & Febiger, 1922.

THIS little volume is a useful addition to the literature which can be utilized as ammunition in campaigns against tuberculosis. A chapter on the cost of tuberculosis compares the public money

spent for prevention and the economic wastage entailed by this disease, and the discussion here is unusually full and frank. In discussing hospitals and sanatoria the analysis is conservative and reasonable. The discussion as a rule steers clear of any question of detail in the treatment of the individual patient and adheres faithfully to the main theme of community problems. There is a chapter on tuberculosis and the nurse (by Miss Billings), and an excellent one on the careless and incorrigible consumptive.

This book should be of interest to physician and layman alike, to the teacher in the public school and to the employer of industrial labor. There is much information contained in its relatively few pages. R. G. T.

THE PRACTICE OF MEDICINE. By A. A. STEVENS, A.M., M.D., Professor of Applied Therapeutics in the University of Pennsylvania, Philadelphia; Professor of Therapeutics and Clinical Medicine in the Woman's Medical College of Pennsylvania. Pp. 1106; 35 illustrations. Philadelphia and London: W. B. Saunders Company, 1922.

THE appearance of a new text-book on medicine would naturally make one think that the subject of "medicine" would be presented in a form somewhat different from that followed without exception by all medical text-books. One would anticipate, as an excuse for bringing out a new work, that at least it would be a book which did not follow the regular form instituted years ago but which would present the subject-matter in a modern manner. On the contrary, the reviewer was doomed to disappointment when he went over the book. The usual structure was followed throughout. Thus the first section dealt with infectious diseases, the next with the intoxications and so, on terminating with the diseases of the nervous system. The diseases in themselves are under the accustomed and expected subheads: Definition, Etiology, Morbid Anatomy, Symptoms, Diagnosis, Prognosis, Treatment. It is difficult to understand just why there should be any particular demand for a book such as this which in no way differs from the usual medical text-book type and of which numerous examples exist. When the reviewer picked up the book he hoped that on account of the long and extensive clinical experience of the author perhaps the subject-matter would be presented as a Mackenzie might present it, with much attention paid to the development of symptoms to the functional disturbances that arise secondarily to disease and to the other similar expressions of bodily disorders upon which much stress is now being laid; but such was not the case. Favorable comment on the book would include the statement that it is up to date. Recently described diseases have been reported and an epitome

at least has been presented of the newer studies of diseases with which we have been acquainted for many years. Unfortunately the references are incomplete and would be valueless unless the prospective seeker for more complete information would go to a considerable amount of trouble to get the correct references. Large numbers of prescriptions are also given. Here it is a question if these are of any real value. In only exceptional cases would the same ingredients and exact proportions in which the prescription is written by an author be given to the expectant patient.

ORGANS OF INTERNAL SECRETION. By IVO GEIKIE COBB, M.D., M.R.C.S., Neurologist, Ministry of Pensions. Third edition. Pp. 352. New York: William Wood & Co., 1921.

THE third edition of Cobb's treatise on the glands of internal secretion is somewhat altered from that of the previous edition by the addition of three new chapters; the bulk of the text, however, remains the same. In going over this book one is struck with the lack of critical study, the general tendency to draw conclusions from insufficient data and the absence of clinical control. The first portion of the book is rational and well presented, but of the latter part of the book the same cannot be said. It seems a pity to recommend to the practitioner, and this book is dedicated to the general practitioner, the idea that "machine-gun" polyglandular preparations should be given for so many and so diverse conditions.

J. H. M., JR.

MANAGEMENT OF THE SICK INFANT. By LANGLEY PORTER, M.D., Professor of Clinical Pediatrics in the University of California Medical School and WILLIAM E. CARTER, M.D., Assistant in Pediatrics and Chief of Out-Patient Department in the University of California Medical School. Pp. 654; 54 illustrations. St. Louis: C. V. Mosby Company, 1922.

THIS book is unique in that it deals exclusively with the peculiarities of disease as it occurs in infants. In the first part of the volume symptoms are discussed. There are ten chapters here dealing with such symptoms as vomiting, diarrhea, constipation, hemorrhage, fever, pain etc. Treatment is also mentioned in these chapters. In part two, various diseases are taken up in an orderly manner. Thus one finds under the different headings and in separate chapters diseases of the respiratory tract, diseases of the digestive tract and diseases of the heart and circulation. Also in this section there are chapters on diseases of

the blood and lymphatics, diseases of the nervous system, skin diseases, genito-urinary diseases, diseases of the osseous system, internal secretions and infectious diseases. It is the third part of the book, that will cause it to assume an important place in the pediatrist's library. Here, in a most clear-cut and concise manner, are described a great many procedures which are of use in the diagnosis and treatment of diseases in infancy. Intravenous injection, intraperitoneal injection, determination of coagulation time, ventricular puncture, temperature taking, gastric lavage and Schick testing are only some of the things mentioned. Even the cistern puncture of Ayer has found a place in the numerous list. Different formulas and recipes are clearly given and also there is a list of drugs and combination of drugs which may be used in the treatment of diseased conditions. The illustrations are good and to the point. This book should prove of great value to the pediatrist and anyone dealing with sick children. A. G. M.

CONTRIBUTIONS FROM THE PEKING UNION MEDICAL COLLEGE, PEKING, CHINA. By HENRY S. HOUGHTON, Director. Vol. I. Pp. 335, N. p., 1921.

THE establishment of a new center of medical research is in itself a matter of world importance; but when this center is in the oldest and yet—medically speaking at least—the most backward civilization in the world and when its personnel and materiel prove themselves capable of a yearly output of worthy original work that requires 335 pages for presentation, then there is double matter for congratulation. Volume I of the *Contributions from the Peking Union Medical College* is a welcome and important addition to that steadily growing group of similar publications issuing from the active research institutions of this country. Their usefulness in a working library has already been commented upon in this journal. May they long continue to flourish and expand!

It is interesting to note that of the twenty-nine articles comprising the Peking volume, nine are on topics in the domain of parasitology and four of hygiene; while anatomy, bacteriology, chemistry, medicine, surgery, ophthalmology, neurology and the history of medicine are represented by one or two papers each. Sixteen of these articles appeared in the *China Medical Journal*. There is also given a list of eighty-nine publications by members of the staff prior to the compilation of this volume. Although distinctions may be invidious in a publication of such a high average level, one cannot refrain from a word of special commendation on Maxwell's article on "Filariasis in China" and Cowdry's two delightful glimpses into Chinese medical history. Congratulations on the first fruits of

this important center of medical education and research that has arisen in the Far East are distinctly in order, and Volume II, which is apparently well under way, will be awaited with lively anticipation.

E. B. K.

MANUAL OF PHYSIOLOGY. By H. WILLOUGHBY LYLE, M.D., F.R.C.S., (Eng.), Examiner in Physiology of the Royal College of Surgeons of England. Pp. 747; 139 illustrations. London: Henry Frowde, Hodder & Stoughton, 1922.

THIS manual was written to give the student a book of medium size which would at the same time be fairly comprehensive. The author had sixteen years' experience as lecturer at King's College, and the present volume embodies the substance of the lectures delivered there. The book is written in a simple, interesting style, and the author is careful to select his phraseology to make clear his meaning. It may be that, at times, his explanations are too simple and transparent, but this is certainly a pedagogic advantage. On the other hand, there are omissions of some topics which should be at least mentioned in a modern physiology. The figures are mostly of gross and microscopic anatomy, with a small number of tracings. The plan of the book is well suited to the average student, and will give him at least one view or theory in fields where the larger books present evidence for several. W. H. F. A.

PRACTICAL INFANT FEEDING. By LEWIS WEBB HILL, Junior Assistant Physician to the Children's Hospital, Boston, and Assistant in Pediatrics, Harvard Medical School. Pp. 483; 32 illustrations. Philadelphia and London: W. B. Saunders Company, 1922.

DR. HILL states that he has tried to write a book which will help practitioners, not only to treat but to understand feeding cases as they occur in his daily practice. This is a laudable aim, because unless there is some knowledge of the underlying principles of physiology and metabolism the mere application of methods of procedure will not be successful in the care of either the well or the sick baby. Throughout the volume the results of scientific investigation which have been of practical importance have been mentioned and applied to practice. The literature has been quite extensively reviewed in the chapter on the physiology and pathology of digestion and nutrition. The second chapter is on the stools in infancy and the next two on human milk and breast feeding. A discussion of the history of modern artificial infant feeding occupies a chapter.

Following this are chapters dealing respectively with cow's milk, modification of cow's milk, special preparations, artificial feeding of the normal infant, digestive and nutritional disturbances in the bottle-fed, idiosyncrasy to cow's milk and the diarrheal diseases. In the feeding of the normal infant four periods are considered: From birth to three weeks; from three weeks to nine months; from nine months to one year; the second year. Foods other than milk are advised at nine months, but not before, and these foods are cereals, beef juice, broths, rice and zwieback. Dr. Hill does not believe that vegetables are necessary in the first year of life. While it is stated that many babies may be fed successfully with whole-milk mixtures from birth, arguments are put forward against their use, and mixtures with a higher fat percentage and a lower protein percentage than would obtain in whole-milk dilutions are recommended until the ninth month of life. The indigestions are simply classified as those due to fat, carbohydrate and protein, and the diarrheas into mechanical, fermentative and infectious. Several chapters consider special subjects, such as constipation, prematurity, rickets, pyloric stenosis, and so on. A. G. M.

AIDS TO ORGANOTHERAPY. By IVO GEIKIE COBB, M.D., M.R.C.S., Neurologist, Minister of Pensions. Pp. 183. New York. William Wood & Company, 1922.

THIS small volume of Cobb's is largely an abridgment of his larger volume which is reviewed in the present number of the JOURNAL. It is prepared as a student's aid. J. H. M., JR.

THE WRITING OF MEDICAL PAPERS. By MAUD H. MELLISH, Editor of the Mayo Clinic Publications. Pp. 157. Philadelphia and London: W. B. Saunders Company, 1922.

A very large number of physicians some time or another in their career attempt to write papers on medical subjects. Many of them do not know how properly to prepare the manuscript for the publishers, and it is for them that this small book is written, as it deals chiefly with how to prepare manuscripts. It also gives some very useful hints on the subject-matter of the hypothetical paper. To one who comes in contact with numerous manuscripts and knows the difficulties under which editors labor this book cannot be too highly recommended. It would be a wonderful assistance to editors if it were in the hands of every medical man who attempts to write. J. H. M., JR.

ANATOMY OF THE BRAIN AND SPINAL CORD. By J. RYLAND WHITAKER, B.A., M.B. (Lond.), Lecturer on Anatomy, Surgeons' Hall, Edinburgh. Fifth edition. Pp. 262; 103 figures. Chicago: Chicago Medical Book Co., 1921.

THIS is a book which has been found useful by many medical students in attaining their first knowledge of the structure of the central nervous system. The subject is treated mainly from the standpoint of gross anatomy. The method used is to present everything in the form of diagrams and to use colors liberally in differentiating the various structures. While this may not give a picture true to nature, it certainly makes a very definite impression on the reader, even the dullest. The illustrations of gross structures are clear and well-executed, and excel those of the cross-sections of the brainstem, which are shown in an extremely diagrammatic manner. There are short directions for dissection, but no methods are given for making microscopic sections. W. H. F. A.

PROTEINS AND THE THEORY OF COLLOIDAL BEHAVIOR. By JACQUES LOEB. The Rockefeller Institute for Medical Research. First edition. Pp. 292; 4 illustrations, 76 curves. New York: McGraw-Hill Book Company, 1922.

THOSE who have followed Jacques Loeb's interesting investigations in colloidal chemistry will welcome his book which presents a systematic review of his work. The book is distinctly argumentative in nature. The author aims to prove two things: First, that protein chemistry is not essentially different from that of crystalloids, and that the laws of stoichiometry are as applicable to the one as to the other; secondly, that Donnan's theory of membrane equilibrium (which states that the unequal concentration of crystalloid ions on opposite sides of a membrane resulting from the unequal distribution of diffusible ions when one nondiffusible ion is present gives rise to potential differences and osmotic forces) offers the best explanation both quantitatively and mathematically for the physical phenomena of colloidal solutions. In clearing his way to these newer theories, the author takes pains to point out the erroneous deductions, such as Freundlich's adsorption formula, Pauli's hydration theory, and the Hofmeister ion series, that were drawn from experimental results in which the fundamental factor (the hydrogen-ion concentration) had not been given proper consideration. The author presents his subject in an aggressive, interesting manner, using numerous simple experiments to illustrate or prove his point. At times one feels, however, that the discussion is unnecessarily protracted, and that certain portions could be considerably condensed without sacrificing clearness. A. J. Q.

A Laboratory Manual for Comparative Vertebrate Anatomy. By Libbie H. Hyman, Ph.D., Department of Zoölogy, University of Chicago. Pp. 380; 69 illustrations. Chicago: The University of Chicago Press, 1922.

This is a companion volume to the laboratory manual for elementary zoölogy previously reviewed in this journal (1920, **159,** 133). The course in comparative anatomy is very important to students preparing for medicine, and this manual gives directions which will serve as a standard. In the student's career in anatomy there is usually a gap between his pre-medical and his medical work, so that he does not carry over into the medical school the knowledge he has acquired in his college courses. And consequently, while he has a great deal of information, he is not able to make proper use of it. A contributing factor to this state of affairs is that while the human anatomist and the comparative anatomist may be experts, each in his own field, they are not usually masters of both branches. In consequence, the teacher of one branch makes but casual reference to the other field. Such a book as this, if carefully followed and studied, will clarify the student's vision and help to guide him through the intricacies of human anatomy. The subject is treated on the comparative plan: One system at a time is studied in a series of animals, such as a fish, amphibian, reptile and mammal. In all, seven systems or groups of organs are considered, in addition to the external features. Of these, the circulatory system and the endoskeleton are described at the greatest length. The descriptions have been written from the specimens while the dissections were being made, and show the greatest attention to detail. A short account of the development and evolution of each system is included with its description, and constitutes a useful feature of the book. W. H. F. A.

Obstetrical Nursing. By Carolyn Conant Van Blarcom, R.N., formerly, Assistant Superintendent and Instructor in Obstetrical Nursing, Johns Hopkins Hospital Training School for Nurses. Pp. 546; 208 illustrations. New York: The Macmillan Company, 1922.

In contradistinction to the average text-book on obstetrical nursing, which so often describes only the personal ideas of the author and the technic of his particular maternity hospital in a rather narrow manner, the volume at hand by Miss Van Blarcom is offered after an extensive survey and study of the methods and measures used in various maternity centers. There is gained thereby for the text a wider outlook and a broader scope than is

usually found. The principles of obstetrical nursing are presented in a pleasing and comprehensive manner. The addition of the forms, rules and directions for care of obstetric patients used by several public health associations should enhance the value of the book to the community nurse or visiting nursing aide.

The illustrations are excellent; many are from well-executed photographs and supplement the text in a graphic manner. The chapter on nutrition of the mother and baby is an innovation in such a book. The scientific side of the question seems to have been too greatly stressed for the average nurse. P. F. W.

THE PRACTICE OF MEDICINE IN THE TROPICS. Edited by W. BYAM, O.B.E., Lecturer on Tropical Medicine at St. George's Hospital Medical School and R. G. ARCHIBALD, D.S.O., Director, Welcome Tropical Research Laboratories, Sudan Government, Gordon College, Khartoum. Volume I. Pp. 856; 334 illustrations. London: Henry Frowde, Hodder & Stoughton, 1921.

THE first volume of a very portentous reference text-book contains almost entirely what might be called the preliminary phases of tropical medicine; that is to say, it is composed of sections on hygiene and minor sanitation, on nursing in the tropics, on entomology, on laboratory methods, on snakes and snake poisoning, and on toxicology. All these various sections are most complete and well presented. The section on sanitation, for example, contains nearly two hundred pages; it seems to be very well executed. The section on laboratory methods is also carefully compiled: One portion of it, on transfusion of blood, is a copy of the method used in the American army during the war and published by the American Red Cross in France. If the subsequent volumes of this work are as carefully gotten up as the first volume, then, to the English-speaking profession, there has been presented a notable work and one which will offer to the physician practising in the tropics or subtropics a treatise on the diseases indigenous to those climates which will be unsurpassed in the English Language.

J. H. M., JR.

A TREATISE ON GLAUCOMA. By ROBERT HENRY ELLIOTT, M.D., B.S., Sc.D., F.R.S.C., late Superintendent of the Government Ophthalmic Hospital, Madras; Ophthalmic Surgeon to the Seamen's Hospital Society. Second edition. Pp. 650; 213 illustrations. London: Henry Frowde, Hodder & Stoughton, 1922.

THE early chapters of this book are devoted to the subject of the secretion of the intraocular fluid and its excretion from the

eye under normal and abnormal conditions. A review of the experimental work so far done on the problems of the intraocular pressure follows. The author very fairly presents the views of other workers in this field and very frankly expresses his own views upon the problems still under discussion.

The latter part of the book is devoted to the pathology of glaucoma and medicinal and operative treatment of glaucomatous eyes. As is to be expected, the sclerocorneal trephine operation is presented in detail and the various other operative procedures for glaucoma are hardly given the space to which they are entitled. The book is well arranged and—even for the reader who is not convinced that the trephine operation is the final answer for the problem of glaucoma—is most valuable and enjoyable.

B. F. B., Jr.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Quinine in Cardiac Disease.—R. SINGER and H. WINTERBERG (*Wien. Arch. f. inn. Med.*, 1921, **8**, 329) report, from Wenckebach's Clinic, results obtained from the extensive use of quinine in cardiovascular conditions. The salts used are the dihydrochloride carbamide of quinine and the bimuriate of quinine. On normal subjects the administration of 2 or 3 grams of quinine in divided doses produces almost constantly a generalized sense of warmth, occasionally dizziness and tinnitis and frequently the bitter quinine taste in the mouth. The physiologic action consists of a moderate acceleration of the pulse and an almost complete disappearance of sinus arrhythmia; there are minor alterations in the form of the electrocardiogram and an increase in rate in cases of sinus bradycardia. The physiologic action in a general way is similar to that of atropine. In "irritable heart" there is a tendency toward improvement in the general condition of the patient and in subjective symptoms. The drug was found of especial value in treatment of precocious systoles, particularly of such as were of ventricular origin and not associated with obvious cardiac disease. Both oral and intravenous routes of administration were found satisfactory. Striking results were obtained in cases of paroxysmal tachycardia treated with 0.5 gm. of quinine sulphate intravenously. After prolonged administration by mouth of small doses of quinine, a reduction was observed in the rate of the auricular waves in a case of flutter. Suggestive results were obtained in instances of hypertension and Cheyne-Stokes respiration. Quinidin is suggested as preferable for use in precocious systoles, flutter and fibrillation of the auricles. Quinine is suggested as a drug to be tried intravenously for obstinate paroxysmal tachycardia that has resisted the simpler methods of approach.

Effect of Hepatic Extract on the Cardiovascular Apparatus.—ROGER (*Presse méd.*, May 24, 1922) reports experimental studies with hepatic extracts which follow a series of observations upon the effect of extracts of various organs upon the heart and cardiovascular apparatus. In the case of hepatic extracts he finds two groups of chemical substances grouped according to their physiologic action. Some are alcohol-soluble and exert a striking vasoconstrictor action. Among the other substances is one that exerts a powerful effect upon the heart, producing a bradycardia of sinus origin. One tracing shows a pulse-rate of less than one-third the normal rate, which followed the injection of hepatic extract into an experimental animal.

A Ten Year Old Strain of Fibroblasts.—EBELING (*Jour. Exp. Med.*, 1922, **35**, 657) describes a strain of fibroblasts obtained from the heart of a chick embryo which has completed the tenth year of its life *in vitro*, during which time it has passed through 1860 generations. The author believes that fibroblasts will proliferate indefinitely, as do colonies of infusoria. During this time the technic of preserving this "potential immortality" has been progressively perfected, and more than 30,000 cultures have been derived from the original fragment. With the development of methods whereby differences of less than 10 per cent in the rate of growth could be detected, these cultures have been used for physiological studies by Carrel, Ebeling, and others. The cells remained indefinitely young or grew old according to the food material which they were given and the extent of the elimination of their catabolic substances. Thus embryonic juice was found to contain a substance which increases the velocity of cell multiplication to a high degree. In the same manner, it was found that adult serum produces an effect opposite to that of embryonic juice. This inhibiting power of a serum increased very much with the age of the animal from which it was obtained. It was also shown that the strain responds to the presence of a foreign protein in the culture medium by becoming immunized against its action. As it has become possible lately to obtain strains of lymphocytes and of epithelial cells living *in vitro* by practically the same procedure that is used for fibroblasts, the scope of these studies will be increased. Several excellent photomicrographs of the proliferating fibroblasts accompany the article.

Studies on Asthma. —LARSON, PADDOCK and ALEXANDER (*Jour. Immunol.*, 1922, **7**, 81) report their observations of bronchial asthma and allied conditions. The work was carried on in the asthma clinic of the Bellevue Hospital, New York City. It embraced the following investigations: (*a*) A continued study of the clinical considerations of asthma, (*b*) observations on skin reactions, and (*c*) effects of vaccine therapy. Briefly from the clinical standpoint the authors emphasize the importance of recognizing bronchial asthma as speedily as possible, eliminating those cases which fall into an entirely different group. They classify their cases as follows: (1) Bronchial asthma, simple and uncomplicated; (2) chronic bronchial infection with its complications simulating bronchial asthma; (3) bronchial asthma, complicated by chronic bronchitis. The first type is very well defined by a typical history suggesting a sensitiveness to a foreign protein. The second type is quite the opposite.

There is no history of allergic conditions. There is a bronchial infection simulating bronchial asthma. The third type is primarily type one, on which infection is superimposed. The immunological studies reveal several important facts. The authors compare the different methods of performing the skin tests. They feel that the intracutaneous method of determining an individual's sensitiveness is far more accurate than the scratch method. In the first place if one is using dry preparations with the scratch method there is no way in which to tell whether they have lost their potency. With solutions, contaminations are easily detected. To compare the two methods a number of known sensitive individuals were tested by the cutaneous and intracutaneous procedures with the same solutions. The experiment reveals that certain individuals, whose asthma is brought on by a specific pollen, fail to react by the scratch method but with an intracutaneous injection a very definite skin reaction occurs. The authors further state that the reaction depends somewhat on the length of the scratch. A long scratch for example gives a broader reaction than a short one. They also are of the opinion that the location of the scratch influences the reaction although they offer no explanation why this should affect it. The reaction is also influenced by the amount of protein brought in contact with the cells, and the amount of solution injected into the skin. With reference to vaccine therapy in asthma, the authors are rather optimistic. They feel that in asthma associated with bronchial infection vaccines, if given with caution, are worth a trial. How these agents act has not been determined, and further study is planned.

Neurorecurrences Following Arsphenamine.—ZIMMERMAN (*Arch. Dermat. and Syph.*, 1922, **5**, 723) reports a study of 39 cases of neurorecurrences (precocious neurosyphilis) following arsphenamine. The material is in large part from the syphilis department of the Johns Hopkins Hospital. He divides the cases into three groups: (1) Acute syphilitic meningitis with or without focal cranial nerve lesions; (2) meningitis of moderate or slight intensity, manifested chiefly by headache and focal lesions; (3) a group in which there are no general symptoms of syphilitic meningitis, the entire complaint being due to a focal lesion. He demonstrates that the facial and auditory nerves are those most frequently involved (in 18 cases), both nerves frequently being involved in the same patient. The clinical details of the author's cases are well summed up in a most exhaustive table. From a study of the literature two groups of neurorecurrences may be differentiated from the pathological standpoint: First, a diffuse meningovascular process, and second, focal lesions involving especially the optic, auditory and facial nerves, without diffuse changes. The first group always presents definite abnormalities in the cytobiology of the cerebrospinal fluid, whereas in the second, the fluid is often normal. Neurorecurrences are to be explained on the basis of resumed activity of temporarily suppressed organisms in a host unable to develop resistance owing to therapeutic interference. The importance of a thorough course of mercury in all cases of early syphilis is emphasized. According to the author, efficient mercurial treatment, administered immediately following arsphenamine, eliminates these serious reactions on the part of the central nervous system as successfully as combined therapy.

The treatment of these cases is briefly discussed. The success of therapy depends, according to the author, almost altogether on how soon treatment can be begun after the onset of neurological symptoms.

Endamœba Dysenteriæ in Hodgkin's Disease.—KEFOID and SWEZY (*Jour. Am. Med. Assn.*, 1922, **78**, 1604) report a case which clinically and pathologically resembled Hodgkin's disease. In the enlarged glands of this patient the authors found cells which they regard as amœba, probably Endamœba dysenteriæ. They base this interpretation on the structure of the nucleus of this cell, particularly as it appeared during mitosis. The most important evidence adduced is the numerical contrast between the number of chromosomes believed to be normal for human cells and the number observed in the abnormal cells. The latter number corresponds to that observed in amebas. The authors suggest the possibility of Hodgkin's disease being amœbiasis of the lymphatic system.

Amœbiasis of the Bones.—KEFOID and SWEZY (*Jour. Am. Med. Assn.*, 1922, **78**, 1602), on similar grounds to those described above, believe that certain ameboid cells found in the bone-marrow in cases of arthritis deformans are true amebas, and they suggest the inference that the organism may be the etiologic factor in Ely's second or non-bacterial type of arthritis deformans.

SURGERY

UNDER THE CHARGE OF

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Decapsulation of the Kidneys in Bright's Disease.—SANDERSON-WELLS (*British Med. Jour.*, December 3, 1921, p. 940) says Edebohl's principles were attacked by physiologists upon these grounds: That the renal arteries are end-arteries and terminal; that the blood supply from the capsule is insignificant; that renal tissue once destroyed does not regenerate; and that chronic nephritis is the local expression of a general disease and a cure must remove the cause. Experimental work upon animals showed that a new capsule was formed in a few weeks thicker and denser than the normal capsule; that there were fewer vessels in the new than in the old. Injections were made into the renal arteries and the aorta with the renal arteries tied. The general opinion as to the result of these experiments was that there was but slight communication. Stursburg, however, found on injecting into the aorta with the renal artery tied that the injection penetrated even to the papillæ. Although the outlook appears disappointing from physiological and pathological aspects, the clinical case reports are excellent.

The uremic patient has been restored to consciousness, while suppression of urine and edema disappear. Patients apparently doomed have returned to work; many have subsequently been pronounced cured by high authorities. The operation therefore deserves consideration under two conditions: First, as an emergency in eclampsia, uremia and suppression of urine; the more desperate the extremity the more certainly it should be discussed; and second, in chronic cases when medical treatment has failed after a thorough trial. In both the above classes the heart and arteries should be reasonably sound, which probably means that most success will be obtained in the first half of life.

The Surgeon as a Pathologist.—BOND (*British Med. Jour.*, December, 1921, p. 973) says that a capacity to elaborate a substance or substances closely allied to, if not identical with, glycogen is possessed by leukocytes, myelocytes, and certain epithelial cells. In the case of the white blood cells, this capacity is in the main limited to the polymorpholeukocytes when they emigrate or escape from the blood stream. In the emigrated leukocyte this glycogenic substance takes the form of a colloid liquid which is rapidly exuded from the cell and gives a delicate mauve color with iodine. In the myeloid cells of the red marrow and in some myeloma cells this substance is also present and is somewhat evanescent. In certain epithelial cells of the mucous membranes which line the orifices of the digestive, respiratory and genito-urinary canals this iodophil substance is present in a more granular and less soluble form. It is more closely incorporated with the cell cytoplasm and stains a red or red-brown color with iodine. The same or an allied substance is also constantly found in certain cancer cells of epithelial origin. In the primary growth it is present in the cells which form the cell nests. In common with the irregular growth of the epithelial cells in the cancer area the disposition of the iodophil cells also undergoes a change. These are reduced in number and are collected in irregular groups rather than in stratified layers. This iodophil substance is also present in the epithelial cancer cells found in the lymph glands and in other secondary deposits. The presence of this capacity for elaborating iodophil substances by cancer cells in secondary deposits is an indication of the retention of some degree of original function by these cells in their abnormal situation and is associated with important problems of cell heredity.

The Treatment of Gastric Ulcer.—MOYNIHAN (*British Med. Jour.*, February 11, 1922, p. 267) says that medical treatment if properly carried out for a sufficiently prolonged period, should enable an ulcer to heal. The need for surgical treatment is a confession that such treatment is unattainable or has failed. The procedures that have been adopted are as follows: Gastroenterostomy; excision of the ulcer; gastroenterostomy combined with excision; gastroenterostomy combined with destruction of the ulcer by cautery (D. C. Balfour's operation); median resection of the stomach (sleeve resection); gastroenterostomy combined with jejunostomy; and partial gastrectomy. This last operation has been most satisfactory for the author. In gastrectomy the mortality in his hands has been 2 per cent. The quality of recovery is excellent. Secondary operation was necessary only once in a series of ten years' duration. There has only been one

unsatisfactory result in this group of 118 cases, a young woman from whom the author removed the stomach for chronic ulceration of the lesser curvature. A group of tuberculous mesenteric lymph nodes were also taken out. Since operation intermittent attacks of diarrhea have occurred with temporary wasting. In none has there been the development of carcinoma or a return of ulceration.

Epididymitis and Suprapubic Prostatectomy.—WHITE (*Lancet*, February 18, 1922, p. 321) says that inflammatory changes in the epididymis as a result of prostatectomy are the rule, for 82 per cent of cases studied gave this result. Five degrees of inflammation were recognized ranging from mere thickening of the epididymis to pus formation involving the adjoining testicle in slough. The inflammation may be unilateral or bilateral. It is generally more advanced in one side than the other. The amount of sepsis in the prostatic cavity is a very important point in determining the degree of epididymitis, for the prostatic cavity is cup shaped with very imperfect drainage. Moreover the torn ends of the ejaculatory ducts in the posterior wall of the cavity are continuously in contact with infected material.

Aberrant Adenoid Cystic Epitheliomas.—JOHNSTON (*Ann. Surg.*, 1922, **75**, 331) says that adenoid cystic epitheliomas of the salivary gland type occurring in the tissues of the mouth and face are not as uncommon as the literature would indicate. Such neoplasms have been reported but not properly recognized and histologically interpreted. The tendency is to regard them as sarcomas. To this fact may be attributed some startling surgical cures. The characteristic tumor has slight malignant properties. Therefore it does not ulcerate and invade in its early stage. Radium treatment has been entirely successful in these cases.

Pathology of Lung Suppuration.—ASCHNER (*Ann. Surg.*, 1922, **75**, 321) says that lung suppurations may be divided into bronchiectasis, a general disease of the bronchi in one or more lobes (bronchiectatic abscess is a localized suppurative process in the course of a bronchus and thus far observed only in post-tonsillectomy cases), suppurative pneumonitis, a diffuse purulent process. Certain interesting histological changes have been observed: metaplasia in bronchial epithelium; epithelial lining of bronchiectatic abscess and proliferation of smaller bronchioles and air passages resembling proliferation of bile passages in portal cirrhosis.

The Influence upon Toxicity and Trypanocidal Activity of Shaking Acid and Alkalinized Solutions of Arsphenamine and Solutions of Neoarsphenamine in Air.—SCHAMBERG, KOLMER and RAIZISS (*Am. Jour. Syph.*, 1922, **2**, 1) say that the undue shaking of alkalinized solution of arsphenamine increases the toxicity; the shaking of such solutions is rarely necessary. The shaking of acid solutions of arsphenamine for one minute beyond the time necessary to effect solution is accompanied by a slight increase in toxicity. Ten minutes' extra shaking increases the toxicity still further. The shaking of solutions of neoarsphenamin for even such short periods as one minute is accompanied by a great increase in toxicity. Shaking for ten minutes enormously

increases the toxicity. It would appear from the studies of Roth and from those which the authors have conducted that neoarsphenamine should be dissolved with as little agitation and exposure to air as possible. The trypanocidal power of acid solutions of arsphenamine is considerably increased after one minute of shaking but is decreased after ten minutes' shaking. The trypanocidal power of alkaline solutions of arsphenamine is considerably increased at the end of one minute's shaking and the increase is still evident after ten minutes' shaking. The explanation of the increase in trypanocidal power is probably to be found in the formation of arsenoxide, which is known to exert a greater trypanocidal and spirocheticidal effect than arsphenamine. The shaking of solutions of neoarsphenamine is not accompanied by increase in trypanocidal effect.

Resection of the Lungs for Suppurative Infections.—LILIENTHAL (*Ann. Surg.*, 1922, **75**, 257) says that chronic pulmonary suppurations wholly or partially of the bronchiectatic type are rarely curable without the extirpation of the pathological focus. The surgical removal of a single pulmonary lobe for chronic pus infection has a mortality of about 42 per cent. The danger is much greater when more than one lobe is infected or in the presence of other complications. Remissions of weeks or even months may occur spontaneously. Palliative operations may be followed by improvement, rarely by apparent cures. The commonest cause of the disease is infection due to aspiration of infected material during tonsillectomy. Radial operation should not be undertaken short of several months after the onset unless the disease is obviously spreading.

Malignancy in Exstrophy of the Bladder.—SCHOLL (*Ann. Surg.*, 1922, **75**, 365) says that exstrophied bladders that are subject to constant irritation and trauma have an extensive glandular covering, the result either of metaplasia from the normal covering or of hyperplasia of glands in the mucosa. Such glandular structure often shows characteristics approximating malignancy. In nine cases of exstrophied bladder in which material for histologic study was available, two were definitely malignant and two showed a typical cellular formation varying markedly from the normal. In the reported cases of malignancy of exstrophied bladders which are relatively frequent the growths were adenocarcinomas. This glandular malignancy is the type that would develop from irritation and hyperplasia of glandular structures.

Sarcoma of the Long Bones.—MEYERDING (*Surg., Gynec. and Obst.*, 1922, **34**, 321) says that 35 per cent of the patients were inoperable or refused operation. In many instances, undoubtedly early diagnosis would have given the patients a chance for a cure. Thirty-two of the 35 patients who died had amputations. The most malignant sarcomata were the osteosarcomata. Eight of these patients lived seven months after operation on the average. Ten patients have died who had excision and cautery. Five died of pulmonary metastasis. The principal points to be decided before operating are malignancy, metastasis, and the extent of bone involved. With early diagnosis, with care to exclude patients with metastasis, and with the use of radium and Coley's toxin, prolongation of life may be looked for following operation.

PEDIATRICS

UNDER THE CHARGE OF

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Congenital Obstruction of the Duodenum.—SCHRODER (*Jour. Am. Med. Assn.*, 1922, **78**, 1039) reports a case in which this condition existed. He says that the most confusing thing is the differential diagnosis from pyloric stenosis. Forcible vomiting, gastric peristaltic waves, the presence in the stomach of the entire previous feeding, and absence of milk stools occur in both conditions. Bile in the vomitus may be absent in duodenal obstruction if the obstruction is above the duct as usually happens. A mass may be felt in both conditions, the dilated and hypertrophied muscle in the ring and wall giving the sensation to the palpating hand. The author had this experience as did others who have reported this condition. If the precaution is taken of using the barium meal and the fluoroscope to supplement the clinical findings, an early diagnosis becomes possible, and operation may save some of these infants. Up to the present there seem to be only two successful operations on record, one in a child of eight weeks and the other in one ten days old. An early gastroenterostomy is the operation of choice, although one of the successful cases on record was cured by a duodenoenteroanastomosis, which is the ideal operation if it is possible to use it. The fixation of the duodenum makes it a difficult proceeding. In the case here reported the diagnosis could not be made from the external inspection at the time of the first operation, which was performed upon the diagnosis of pyloric stenosis. Later after fluoroscopic studies a jejunostomy was done, and would have been of great benefit in an older child. There was probably leakage from the wound as the cause of the poor result. It seems probable that had the diagnosis been made at the time of the first operation the chance for success with a gastrojejunostomy would have been fair.

Chronic Arthropathy.—HYMAN and HERRICK (*Jour. Am. Med. Assn.*, 1922, **78**, 1043) report a case in an infant of twenty-eight months in which the most striking thing on examination was the marked thickening of all the long bones, and the clubbing of the fingers and toes. In this child congenital syphilis was ruled out by the absence of any suggestive family or past history, by two negative Wassermann tests, and by the absence of any clinical evidence of syphilis. Rickets did not seem to be a reasonable explanation of the extensive thickening of the shafts of the long bones when the epiphyses did not give the appearance of the epiphyses in rickets. The roentgenograms were similar in many respects to those seen in infntile scurvy, particularly in the suggestion of Trümmer's zone at the lower end of the tibiæ. This disease could not explain the clubbed fingers and toes, and the bone changes of the metacarpals and distal phalanges as seen in this child. Careful review of the history did not reveal anything suggestive of scurvy during the

first twenty-two months of life, and after that time the diet had been under careful supervision. It seems likely that the line of increased density just above the epiphysis of the lower end of each tibia was due to some metabolic disturbance other than scurvy. It was extremely interesting to note that the periosteal thickening in the phalanges and metacarpal bones took place during the last four months of observation.

The School Child before and after Tonsil and Adenoid Removal.—DAVIS (*Jour. Am. Med. Assn.*, 1922, **78**, 1187) divided the children to be studied into two main groups: Group I comprised about 6000 children from six, twelve or fourteen years of age, and Group II included about 1500 children from twelve to eighteen years of age. From each of these groups were taken the children with enlarged tonsils and adenoids, and the children who had been operated on for removal of these structures. Only markedly enlarged or obstructing tonsils and those usually termed diseased tonsils were included. Local causes of poor breathing, such as deviated septum, enlarged turbinates, polyps and the like, were eliminated as much as possible, and all were given the same routine examination. About 5 per cent of the total number of children had been operated on for the removal of tonsils in each group. In Group I there were recorded 450 pronounced tonsil and adenoid cases, or about 7.5 per cent of the total number examined. One hundred, or 22 per cent of this number, had enlarged cervical glands and 9, or 2 per cent had cardiac murmurs at the apex. All the children with enlarged adenoids were bad breathers. In this group there were 296 children who had had their tonsils and adenoids removed with breathing good in 132, or 44 per cent; fair in 67, or 22 per cent; and poor in 97, or 34 per cent. Of these 296 children 114, or 38 per cent, had enlarged cervical lymph glands, and 10, or 3.5 per cent, had apical cardiac murmurs. A large number of the children had varying degrees of gland tissue proliferation in the pharynx and about the tonsil spaces. Some gave undoubted signs of syphilis. Some were asthmatic and subject to recurrent bronchitis and irritation of the upper respiratory tracts, and others were eczematous. In Group II, 21 children were referred for operations. This is about 1.5 per cent as compared with 7.5 per cent in the other group. Twenty per cent of these had enlarged cervical glands, and none showed heart murmurs. Of the 93 children in this group whose tonsils had been removed, breathing was good in 57, or 62 per cent; fair in 19, or 20 per cent; and poor in 17, or 18 per cent. While 34 per cent of the younger children who had removals breathed poorly, the older group showed only 18 per cent. This was probably due to the older children having reached a stage of immunity to infections, and also to the increasing size of the air space with dehydration and cessation of growth of lymphatic tissue. Twenty-five per cent of the children of this group had enlarged cervical glands, and there were 5 cases of heart disease, or 5.3 per cent. The incidence of heart disease is really very low.

The Clinical Findings in the Normal Chest of the Child.—AUSTRIAN, LANDIS and BLACKFAN (*Report of the Committee on Medical Research, Natl. Tuberculosis Assn.*, May 6, 1922) state that the data obtained on percussion and auscultation of the lungs of normal children show wide variations from a fixed standard. These variations are usual and are

considered to be within normal limits. Inasmuch as these changes are dependent upon alterations that persist as the remains of past infections of the respiratory tract, it is obvious that a careful history with special reference to all infections is necessary if diagnostic errors are to be avoided. Even careful histories must be considered with judgment, as minor infections are soon forgotten by many, and among the less intelligent even more significant illnesses are not recalled. Failure properly to evaluate these deviations from a fixed standard often lead to unwarranted diagnosis of disease and even less justifiable treatment. With a proper appreciation of the widest variations that the normal may present the informed clinician can better understand the findings of the roentgenologist, and each coöperating with the other is less liable to error. D'Espine's sign as indicative of enlarged tracheo-bronchial lymph nodes is of little value. Recognition of and familiarity with these data is of cardinal and practical importance to every patient. Without a proper appreciation of these facts no intelligent differentiation between a normal and an abnormal respiratory tract can be made.

The Use of the Carbon Arc Light in the Prevention and Cure of Rickets.—HESS and UNGER (*Jour. Am. Med. Assn.*, 1922, **78**, 1596) experienced that in the winter, and especially in the early spring, rickets develops on every diet. It is generally mild and overlooked, but if routine clinical, roentgenological, and chemical examinations are carried out, it is surprising what a small proportion of bottle-fed infants will be found to have escaped rickets by March or April. They have also found that rickets is not limited to the artificially fed infant. A recent survey of breast-fed infants showed that by the end of March about one-half showed definite roentgenological evidence of rickets. The infants that they treated by the carbon arc light had been on standard diets, including raw certified milk, dry milk, malt soup and protein milk. All received orange juice daily. Huldschinsky and others had used the mercury vapor quartz lamp for this purpose. The rays which this lamp emits are rich in ultraviolet, but its spectrum differs markedly from that of the sun, in that it is discontinuous, and that much of its ultraviolet rays are of wave lengths considerably shorter than those of the sun. For these reasons it was deemed worth while to try the effect of the white flame carbon arc lamp, which more nearly approaches the sun's spectrum. The fact that this lamp is very rich in luminous rays was another reason for testing its therapeutic value, for it seemed that it might provide illumination at the same time as therapy. The infants entirely naked were placed at a distance varying from three to nine feet from the lamp, and were provided with spectacles or other covering for the eyes. This form of irradiation does not lead to any tanning of the skin. This shows that pigmentation is not an essential factor in heliotherapy of rickets. In every instance there was a subsidence of the rickets, which was evident by roentgen ray often after daily exposures for only two weeks. This consisted in calcification of the lower epiphyses of the radius and the ulnar, which increased progressively as the treatment was continued. Accompanying these changes there was the constant increase in the inorganic phosphate of the blood, which in some cases had a tendency to fall after heliotherapy was discontinued. The carbon arc lamp was found in the laboratory

as well as in the clinic to be a very effective agent in the prevention and cure of rickets. It is comparatively inexpensive, and its rays are not irritating to the skin, so that it can be used for hours with perfect safety. The use of the lamp has the advantage over heliotherapy in that it can be used in the winter months when the tendency toward the development of rickets is the greatest, and when it is not possible to apply heliotherapy on account of the impossibility of exposing the body of the child to the direct rays of the sun at this season of the year.

The X-ray Findings in the Normal Chest of the Child.—PANCOAST, DUNHAM and BAETJER (*Report of the Committee on Medical Research, Natl. Tuberculosis Assn.*, May 6, 1922) found that the normal chest of the child is subject to such wide variations from the roentgenologic point of view as to be beyond the possibility of exact description. The conglomerate shadow, commonly called the hilum shadow, when found lying entirely within the inner third or zone of the lung can be entirely disregarded, or regarded as normal except where it is made up of a solid mass of homogeneous shadow, showing undoubted evidence that it represents a growth or mediastinal pleurisy. Calcified nodes at the root of the lung, without evidence of lung disease, are of no significance except as possible evidence of some healed inflammatory condition, possibly but not necessarily tuberculosis. They are a common finding in the normal chest. In the normal lung the bronchial trunk shadows are not visible in the extreme apical regions. For convenience of description the remainder of the lung is divided into three vertical zones, extending outward from the lateral border of the spinal shadow to the lateral chest wall. The inner zone contains the root shadows. The midzone contains the trunk shadows, gradually fading out into their final subdivisions. The peripheral zone contains radiating lines from these and fading off before the periphery is reached. Where in the midzone or peripheral zone these shadows do not disappear in the characteristic fashion described, the appearance may be evidence of a variety of conditions, past or present, of an inflammatory nature or otherwise. It may accompany a tuberculous process, but is not necessarily indicative of tuberculosis. They feel that the use of such terms as peribronchial tuberculosis and parenchyma tuberculosis should not be used in the interpretation of roentgenograms of the chest. Also they feel that until corroborated by laboratory or clinical findings the use of such terms as active and quiescent should not be definitely applied to evident lesions demonstrated on plates.

The Diagnosis, Prognosis and Early Treatment of Poliomyelitis.—LOVETT (*Jour. Am. Med. Assn.*, 1922, **78**, 1607) points out that it is commonly known that many cases of poliomyelitis are overlooked in the early stages, being incorrectly diagnosed as all sorts of febrile affections, and the diagnosis is usually cleared up only after the paralysis develops. Laboratory diagnosis can be made in the early stages by spinal tapping. The fluid in the acute stages of the disease is clear and colorless, and does not show great increase of pressure. In the first week there is an increase in the cells, due to mononuclear cells of various types, of which the lymphocyte is the most common. The cells may increase to as many as from 1000 to 2000 per cubic millimeter. The

globulin reaction, which is weak at first, increases to its maximum by the end of the third week. The only difficulty in the laboratory diagnosis is between poliomyelitis and tuberculous meningitis. The diagnosis from clinical symptoms is very important as the facilities for laboratory examination are not always available. This cannot be made from the history. Trauma cannot cause this disease. A moderate or high fever occurring suddenly without known cause and accompanied by symptoms in the gastrointestinal or respiratory tracts is suspicious, especially between June and November. The most suspicious symptom of all is stiffness at the back of the neck in attempts to flex the head, but there is nothing really characteristic about the attack. Occasionally the part that will be paralyzed is affected by prickling or numbness. The paralysis may occur in one or two hours or three or four days from the beginning of the attack. After the first few days the diagnosis is very often only too obvious to those who are familiar with the fundamentals of the affection.

OBSTETRICS

UNDER THE CHARGE OF

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The Results of Cesarean Section from 1911 to 1920 Inclusive.—HOLLAND has undertaken to collect the records of the hospitals of Great Britain regarding Cesarean section in ten years. His totals are: for contracted pelvis, 33,372; for eclampsia and toxemia, 231; for antipartum hemorrhage, 208; for other conditions, 386. In Cesarean section for contracted pelvis, when the mother was not in labor and therefore no attempt to deliver had been made, the maternal mortality was 11.6 per cent; early in labor, 1.8 per cent; late in labor, 10 per cent; after induction of labor, 14 per cent, and after attempts at delivery, 27 per cent. The fetal mortality of cases where forceps had been tried was 27 per cent and the early mortality of children delivered by section after considerable labor was nearly 11 per cent. As might be expected, peritonitis and sepsis were the principal causes of the mother's death. There were 33 cases of operation through the lower uterine segment: 12 of them were extraperitoneal operations with 4 deaths; 20 transperitoneal operations with 1 death. In 46 cases of Cesarean hysterectomy there were 8 deaths. When these cases are analyzed it is found that the cases were severely complicated before operation. With all possible deduction of hysterectomy the maternal mortality of Cesarean operation in cases not in labor was 1.4 per cent; early in labor, 1.8 per cent; late in labor, 9.4 per cent, and after attempt at delivery, 26.5 per cent. The fetal mortality at the time of operation was 3.9 per cent and later on among these children a mortality of 4.2 per cent; the later the operation is performed in labor the higher the fetal death rate, and when the operation is done after

the forceps has failed the fetal death rate is very high. It is interesting to note that the maternal mortality of abdominal Cesarean section as indiscriminately practised for eclampsia is 32 per cent, and in eclampsia and toxemia fetal mortality is 50 per cent among infants dying at the operation and those surviving. The writer speaks of other toxemias of pregnancy and those causing eclampsia which is to our mind a confusion of terms and ideas. Thus in 29 cases of what he calls the albuminuria of pregnancy, a maternal mortality after Cesarean section was 20 per cent. The statistics would have been more valuable if eclampsia and what he calls other toxemias had been placed under one head. In placenta previa the statistics are somewhat confused; thus he speaks of *complete* and *central* with a mortality of 14 per cent; uncomplicated, etc., with a mortality of 9.3 per cent, and "placenta previa" 18 cases, 1 death. Obviously these statistics are not clear. Among his cases were 5 Cesarean hysterectomys with no mortality. The fetal mortality in these cases was low, 7 per cent at labor. Among the children surviving the operation and remaining for some time in the hospital the mortality was 22.3 per cent. Unquestionably the fetal mortality of placenta previa treated by Cesarean section was comparatively low. On using the term accidental hemorrhage, probably to include accidental separation of the normally implanted placenta, the statement is not clearly defined. In 66 cases treated by Cesarean section the maternal mortality was 27 per cent. It is difficult to imagine what concealed and revealed hemorrhage may be, but this is mentioned together with concealed hemorrhage and 68 cases of accidental hemorrhage. When Cesarean hysterectomy and the ordinary simple Cesarean section are compared, or these cases of hemorrhage, the mortality of the former is four times as great as that of the latter. This may be because these cases were complicated at operation. Eighty-six per cent of the children in these anomalous hemorrhages were lost. In the miscellaneous cases of various types, numbering in all 366, mortality varied in accordance with the severity of the complication for which the operation was done. The paper is interesting and valuable for the large number of cases studied and the painstaking effort made to arrive at the true position of Cesarean section as practised at present in the British Empire.

Galactocele.—Grynfeltt and Tzélépoglou (*Gynéc. et obst.*, 1922, **5,** 222) publish a well-illustrated and comprehensive paper upon this subject. They find that the condition known as galactocele is not a primary pathological condition. It is a secondary result of various pathological processes in the mammary gland. From the standpoint of anatomy, several varieties may be distinguished. One, the ectasic, which arises from the dilatation of the milk ducts; second, the interstitial, which is formed by the excessive secretion retained in the connective tissue around the gland substance; third, the adenogalactocele, which is an adenocystic tumor containing milk; fourth, the pyogalactocele, which is a chronic abscess in the milk duct and surrounding tissue. From the standpoint of pathology these conditions may arise in two ways: First, from inflammation, which in accordance with its nature, intensity, location and duration, creates the conditions

necessary for the development of the different varieties; second, from traumatisms which rupture the milk ducts and produce lactorrhagia. In the literature of the subject the most commonly reported is the adenogalactocele. Very frequently a number of factors enter into the pathological condition present, producing complex anatomical varieties which are called mixed galactoceles. The clinical development in a given case varies with the anatomical type—a point of practical interest deserving further investigation. In all cases the knowledge that a galactocele may coexist with an adenofibroma explains the hesitation which obstetricians feel in giving a definite prognosis on any line of treatment.

The Treatments of Placenta Previa by Abdominal Hysterotomy.—Brouha, of Liège (*Gynéc. et obst.*, 1922, **5**, 198) has operated 11 times by Cesarean section for placenta previa. Six of these patients were primiparæ, of whom 4 were operated upon before labor; 1 at the beginning of labor; 1 was at seven months, the remainder at term or very near term. In 1 case complicated by uterine fibroid hysterectomy was performed. Ten of these women recovered, 8 without complications and 2 after some fever. One survived delivery for only four hours. Two of the children died two or three hours after the operation without symptoms, except those of weakness. Of the 2 cases whose recovery was complicated by fever, 1 had infection in the abdominal wound. She was in very bad general health and was operated upon as an emergency without much preparation, but finally made a good recovery. The second patient, recovering with fever, was a young frail primipara, who had a serious hemorrhage at the seventh month, at which time she was placed under the care of a midwife. Hemorrhages occurred at intervals, but were treated by hot douches, containing laudanum. When she was finally examined, it was found that the finger could be carried through the cervix against the placenta, which was central. The examination was followed by profuse hemorrhage, and a tampon was used to check it. As the tampon became soaked, it was replaced and operation was finally done. The patient's convalescence was complicated by fever, although the abdominal wound healed naturally and involution of the uterus proceeded naturally. No evidence could be found of pelvic inflammation. It was thought that an important element in bringing about the cessation of fever was the production of a fixation abscess, which on the twenty-seventh day after operation, obtained a half-pint of pus. The case ending fatally was a primipara, aged thirty-four. She had had some hemorrhage during pregnancy, but when near term was taken with a profuse bleeding which rapidly made her anemic. There was slight dilatation of the cervix, but it remained very hard, with the placenta covering the lower segment. The patient had rallied from the operation seeming in unusually good condition, when suddenly her pulse became worse and she died from rapid dilatation of the heart. The writer is in favor of Cesarean section for placenta previa in a large proportion of cases.

Hysteropexy and Gestation.—Rosner (*Gynéc. et obst.*, 1922, **5**, 185) reports the case of a patient aged thirty, the mother of three chil-

dren, who had been operated upon in 1920 for prolapse and retroflexion of the uterus. Anterior and posterior colporrhaphy, a plastic operation on the perineum and hysteropexy, had been performed. About two months after the operation the patient became pregnant, and during the third month of her pregnancy she suffered greatly from pain in the lower part of the abdomen, which pain finally became unendurable. At five months the uterus was very sharply anteverted, the fundus fixed behind the symphysis, and the posterior wall of the uterus distended. The round ligaments could not be made out with bimanual examination. The uterus seemed to be in a sort of sac formed by the edges and tendons of the recti muscles. There was great pain on pressure. On vaginal examination, the cervix was very high up, carried far back; the uterus could not be pushed up by vaginal manipulation. The situation was such that the child could only develop by distending the posterior wall of the uterus, and the patient's suffering was so great that operation was undertaken. On opening the abdomen two adhesions were found which fixed the fundus of the uterus in the neighborhood of the insertion of the round ligaments in the abdominal wall. These adhesions were tense and covered by peritoneum. Without disturbing the uterus these adhesions were severed without much hemorrhage. The points of incision were covered by peritoneum and the abdomen closed. The patient made an uninterrupted recovery, and the uterus developed normally. The patient was examined three times before full term. The uterus grew normally in size; at the tenth month the cervix was in normal position and the head of the child engaged in the pelvic brim. It was not difficult to recognize the fact that the development of the anterior wall of the uterus had been retarded by the fixation operation; while the posterior wall of the uterus had been overdistended. Labor occurred spontaneously at term with slight laceration of the vaginal wall and perineum. The weight of the child was normal, the mother making a good recovery.

Eclampsia Post Partum Apparently Cured by Decapsulation of the Kidneys.—Fey (*Monatschr. f. Geburtsh.*, 1922, **56**, 256) states tnat he has had good results in the use of drugs in the control of eclamptic patients. In the following case, however, he resorted to operation. The patient was aged thirty-six, and had previously given spontaneous birth to two living female children with an interval of about two years. Seven years later she had an abortion at three months. In the pregnancy under consideration the patient was fairly well in the early months, but as the later months approached she had swelling of the legs, headache and sought medical advice. She entered the hospital and gave spontaneous birth to a living male child. Early on the following morning she had eclamptic convulsions with a very small secretion of dark brown urine, containing albumin, casts and red blood cells. The patient was unconscious and her blood-pressure high. The lower extremities became edematous; the breathing was stertorous; five hours after the first convulsion 250 cc. of blood was taken. As the patient did not essentially improve, she was subjected to decapsulation of both kidneys. The kidneys were found large and hyperemic; the capsule of the kidneys was very firm and tense, and when it was incised there was profuse bleeding, especially from the left kidney, but no protrusion

of kidney substance. When the capsules were stripped back the parenchyma was found to be not pale and anemic, as has been stated by some, but very hyperemic. As there was free bleeding on the left side, a tampon of iodoform gauze was introduced. Convulsions ceased after the operation; consciousness and memory gradually returned; the quantity of urine markedly increased, and albumin and casts almost disappeared. Urinary fistulas developed on both sides but eventually closed. Unfortunately at five weeks the child died of pneumonia and convulsions, but the mother made a good recovery.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Erythropoietic Action of Germanium Dioxide.—Maintaining exact conditions of control, HAMMETT, NOWREY and MÜLLER (*Jour. Exper. Med.*, 1922, **35**, 173) injected a sterile 0.4 per cent solution of germanium dioxide into four lots of male and female albino rats. Two lots received in four doses at intervals of four days a total of 6.6 mg. per kilo of body weight and the other two were given 45 mg. in three doses at similar intervals. Weekly determinations of the erythrocyte and leukocyte counts of the blood were made seven days apart. It was found that all of the test rats responded to the germanium dioxide by a marked and sustained rise of from one to nearly five millions in the number of erythrocytes in the blood. Those rats which showed a lower initial count responded better, and *vice versa*. There was no indication that the larger doses of germanium dioxide exerted a greater stimulating effect on the production of the resultant erythrocythemia than the smaller doses. Evidently the effect appeared quickly, the red cell count rising within a week after two injections. The coagulability of the blood became increased while color changes were noted in the liver and bone marrow. In a second communication, HAMMETT and NOWREY (*Jour. Exper. Med.*, 1922, **35**, 507) reported the results of a histological comparison of the liver, spleen, bone marrow, circulating young erythrocytes and differential counts in the albino rats receiving germanium dioxide, with their litter controls. It was found that while the livers of the test animals showed a capillary dilatation and engorgement, and the spleens were more congested than in the controls, there was no evidence of red-cell formation in these organs. In the bone marrow, however, there was evidence of a marked stimulation in formation of nucleated erythrocytes, as well as an increase in the young red cells in

the circulating blood. No noteworthy differences in the values for the various types of leukocytes in the circulation, as determined by differential counts, could be found. The authors conclude from their experiments that germanium dioxide is a potent erythropoietic agent and that the source of the erythrocythemia is the increased production of red-cell precursors by the bone marrow.

The Internal Secretion of the Pancreas.—With the knowledge that since the acinous but not the islet tissue of the pancreas degenerates after ligation of the pancreatic ducts, and assuming that trypsinogen or its derivatives was antagonistic to the internal secretion of the gland, BANTING and BEST (*Jour. Lab. and Clin. Med.*, 1922, **7**, 25), working in conjunction with J. J.R. MACLEOD, have conducted certain experiments on dogs in an attempt to prepare an active extract of the island of Langerhans. The pancreatic ducts were ligated for ten weeks, to allow complete degeneration of the acinous tissue, after which interval the degenerated pancreas was quickly removed under chloroform anesthesia and the extract prepared by slicing into a chilled mortar containing Ringer's solution and partially freezing the tissue. The half-frozen gland was then macerated and filtered, and the filtrate, now at body temperature, was injected into eight to sixteen month old dogs depancreatized by the Hédon method or at the initial operation. The results of various experiments on six dogs are shown in detail with the aid of charts. Over seventy-five doses of extract from degenerated pancreatic tissue have been administered to ten different diabetic animals. It was found that intravenous injections of the extract invariably reduced the percentage of sugar of the blood and the amount of sugar excreted in the urine, the extent and duration of the reduction varying directly with the quantity of the extract injected. Rectal injections were not effective and pancreatic juice destroyed the active principle of the extract and boiled extract produced no effect on the reduction of blood sugar. Extracts made 0.1 per cent acid were effectual, however, in lowering the blood sugar, and extracts prepared in neutral saline and kept in cold storage remained potent for at least seven days. The presence of the extract enabled a diabetic animal to retain a much greater percentage of injected sugar than it would otherwise. That the reducing action was not a dilution phenomenon was indicated by the fact that the hemoglobin estimations before and after injections of the extract were the same, that administration of large amounts of saline did not effect the blood sugar and that similar quantities of extracts of other tissue did not cause the reduction of blood sugar. The authors are convinced that the extract contains the internal secretion of the pancreas, which is the factor operative in controlling carbohydrate metabolism; but they feel that the results of their "experimental work," which certainly appear to mark an epoch in our understanding of diabetes mellitus, "as reported in this paper, do not at present justify the therapeutic administration of degenerated gland extracts to cases in the clinic."

The Diagnosis of Syphilis in Malarial Subjects by the Wassermann Reaction.—JOHNSON (*Jour. Path. and Bacteriol.*, 1921, **24**, 145) reported the results of 738 complement-fixation tests for syphilis on 74 cases of

malaria, all of which were under treatment with quinine (20 to 30 grains daily). The tests consisted of the original Wassermann (using two M. H. D. of complement), Tschernogobouw's modification, Fleming's modification and the Hecht-Fleming method. In 19 cases the first blood specimen was collected during an actual rigor or at a short interval after a rigor, in 45 there was no record of rigor but the first specimen was obtained when the parasites were found in peripheral blood and in 10 cases the blood was collected when no parasites were found but typical relapses subsequently developed with parasites in the finger blood. All cases clinically syphilis or giving a history of previous syphilitic infection were excluded. On retesting the bloods only 7 per cent were found to give positive Wassermann reactions. These investigations indicate that the blood in active benign tertian, malignant subtertian and mixed malaria does not give a positive Wassermann reaction; that positive findings are due to syphilitic infection or to certain factors in the technic employed or to non-specific changes in the patient's serum; that in such cases the serum should be retested and that a positive reaction confirmed by a subsequent test is evidence of luetic infection.

The Wassermann Reaction in Relapsing Fever.—Out of 18 cases of relapsing fever, ROAF (*British Jour. Exper. Path.*, 1922, **3**, 59) found 11 positive to the Wassermann reaction (Emery's and Fleming's modifications) at some stage of the disease, but 6 of the 7 negative cases were tested only once. Excluding 2 of the positive cases in which the test was not repeated, 3 out of 9 persisted during the period of observation (seventeen to twenty days), while all others had become negative eight to thirteen days after the onset of the fever. Two cases were negative on first examination, but became positive three and six days after onset. As a result of these observations the author believes that a transient positive Wassermann reaction may be found as a constant phenomenon during the acute stage of relapsing fever; that the transient character distinguishes it from the reaction due to syphilis, and if the positive result persists in a given case, syphilis may be suspected also.

Digestion of the Esophagus as a Cause of Postoperative and Other Forms of Hematemesis.—PRINGLE, STEWART and TEACHER (*Jour. Path. and Bacteriol.*, 1921 **24**, 396) call attention to the fact that, in all probability, many of the cases interpreted as postmortem digestion of the esophagus have, in reality, an origin during life and report 18 cases, 16 of which were fatal. Ten of the cases were surgical in nature, 2 were associated with accidents and 6 with medical diseases. The outstanding clinical feature was vomiting of black or brown material, twenty-four to thirty-six hours before death, this symptom being found on 13 occasions. In the esophagus itself two striking and distinctive phenomena consist in the presence of black sloughs indicative of intense congestion and hemorrhage and the contrast between the broken-down esophagus and the stomach which is either totally free from digestion or only slightly digested. Two of the cases showed a slight involvement, 7 presented extensive ulcerations and 9 had perforated with widespread destruction of the lower portion of the esophagus. Hemorrhages are always present in the esophageal wall and sometimes in the lungs and pleuræ. Microscopically the condition is a severe ulceration

attended by necrosis, solution of tissue and an acute inflammatory reaction. The authors believe that the condition is not rare, that it is not an agonal manifestation, "but one the nature of which can be diagnosed during life and which might be amenable to treatment."

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Typhus Fever on the San Juan Indian Reservation, 1920 and 1921.—ARMSTRONG (*Public Health Reports*, 1922, **37**, 685) reports on an outbreak which resulted in 63 cases and 27 deaths on an Indian Reservation in the arid Southwest. The epidemic occurred among an Indian population showing 90 to 100 per cent infestation with head and body lice. The infection was probably introduced by laborers from Mexico. The early cases were variously diagnosed as influenza, measles and typhoid fever. The infection existed for about six months before being recognized. The problems of control were made more difficult by the isolation of the affected region, poor roads and scarcity of fuel and water. Delousing was accomplished by the application of a mixture of kerosene and gasoline, the use of a solution of nicotine, 1 : 1000, and by steam and boiling in the case of fomites. An emulsion of kerosene 2 parts, soap 1 part, and water 4 parts was also used to advantage for the body and hair. Cases were in general isolated in their own homes.

Experimental Studies on Tuberculous Infection.—KRAUSE (*Am. Rev. Tuberc.*, 1922, **6**, 1) confirms his belief in the Cohnheim-Cornet-Ribbert Law of Localization, in view of a constantly recurring demonstration provided by infection of a culture of low virulence known as R. l. Krause emphasizes his belief that at its culmination every case of tuberculosis represents, in some degree, the fruition of a long sequence of accidental circumstances. Krause has made a careful study of the course of tubercle bacilli from the path of entry to the lungs in guinea-pigs and rabbits. He has shown that in the guinea-pig the tracheo-bronchial nodes show gross tubercle earlier than the lungs. In rabbits, on the other hand, he generally finds marked involvement of the lungs with slight or only moderate infection of the tracheo-bronchial nodes. Between the microscopic structure of the normal lungs of guinea-pigs and rabbits, there are important differences, which would permit tubercle bacilli to pass through the lungs of the guinea-pigs on to the

tracheo-bronchial nodes, but would tend to retain them in the lungs of the rabbit. Krause states that while the bloodvessels are potent factors in the spread of infection, they act merely as conveyers of bacilli. The real site of the pathologic development of tubercle would appear to be in the lymphatic system, in accordance with the view of Calmette. From mucous membrane the bacillus makes its way into the lymphatic system; and from plugged capillary it does likewise. Where it will focalize is determined largely by lymphatic anatomy (and, therefore, lymphatic physiology); and variations in lymphatic anatomy will determine differences in focalization. Krause has shown that fundamental anatomical differences are actualities which give point to Tendeloo's views of tuberculous focalization, based on physiological inquiries; though he is not inclined to follow Tendeloo all the way, and especially not in regard to non-continuous infection against the lymph stream. With this experimental evidence, he asks a few questions which continually recur to him but which thus far he has not had time or opportunity to investigate in the thorough way which their solution would require. Does human tuberculous infection normally tend to the lung root in early life because then lymphatic drainage is more active and intrapulmonary channels more open and unobstructed than later? In other words, is the child's lung more comparable to that of the guinea-pig, which may be looked upon as constituing one type? With increasing age, do human lungs undergo internal changes which bring them nearer to the type which is normal for rabbits? Does there normally occur an increase and development of intrapulmonary lymphoid tissue over a few years, or through many years? Do formerly open lymphatic paths thus become more or less obstructed, so that bacillary retention within the lung is favored? How much do the inhalation of foreign bodies and the repeated occurrence of respiratory infections alter the puerile lymphatic structure which was once normal? Gardner and Willis have shown that in guinea-pigs the intrapulmonary lymphoid tissues proliferates markedly in response to the irritation of dusts, and that these overdeveloped masses then remain as permanently enlarged structures in the lymphatic paths. Miller has described and figured the same occurrence in man. Dust which is not cast out by the ciliated epithelium comes to be laid down in human lungs along the lymphatics. With increasing age fibroses mark our lungs in varying degree. How much have all these processes to do with bringing about anatomical changes which will tend to arrest bacilli in their lymphatic passage to the nodes and to fix them in the lung itself? Is it not remarkable that even when the adult human lung has massive tuberculosis, the root nodes participate relatively little in the process? Here we have a companion piece to what is normal for the rabbit. What has blocked the relatively easy passage to root which characterizes childhood infection? Krause thinks it is not wholly improbable that the several parts of the lung may differ in details of finer lymphatic structure—in details not fundamental perhaps, yet decisive as regards fixation of bacilli—throughout life or perhaps only at certain periods. May the apical occurrence of localized adult tuberculosis, which is due to relatively slight infection, dependent on such factors? Do we lose our general tendency to lymphatic tuberculosis as we grow older, because with increasing age our lymphatic flow becomes less active and our lymph nodes more

impermeable? A rising incidence of renal and epididymal tuberculosis suggests that age brings no diminution of blood-borne metastases; but wherever the lymphatic apparatus may be conceived as entering into the spread of infection, there is in general much less tuberculosis as childhood passes into adolescence, adolescence to full maturity and completed growth to old age. Krause leaves all these as questions, as phases of a much larger problem, which, he submits, is worthy of attack from the point of departure which he has tried to establish. This is that the determinants of tuberculous infection are almost innumerable; yet among them there exists a very fundamental one which will always bulk large in the shaping of the final result and is comprised in the fact that a varying and variable anatomical structure establishes the loci of infection and to a great extent the further development and progression of infection from these.

Relation of Faulty Cultures to Diphtheria Mortality.—O'KEEFE (*Boston Med. and Surg. Jour.*, 1922, **186**, 603) states that immediately following the common use of diphtheria antitoxin, and after the more general use of bacteriologic diagnosis, the mortality curve of diphtheria took a marked downward trend. As the value of antitoxin became more widely recognized by the profession and public, this curve went lower still. Carey states that in the first decade of the last twenty years the death rate of this disease fell from 43 per 100,000 to 15 and a fraction. He goes on to state that there has, however, been a fairly constant mortality rate during the latter ten years of this twenty-year period. With the advent of toxin-antitoxin administration it is not unreasonable to expect, in the near future, still further lowering of the diphtheria death rate. O'Keefe concludes from his observations that one of the factors in delay of diagnosis of diphtheria is the failure to recognize that unless cultures are properly taken laboratory diagnosis will not be reliable. No amount of care or skill on the part of the bacteriologist can compensate for faulty technic on the part of the practitioner in securing a fair sample of the organisms existing in the membrane or exudate concerned. Twenty-four to forty-eight hours' delay in the administration of antitoxin frequently results, owing to reliance placed upon faultily taken cultures.

Tularemia Francis 1921, Six Cases of Tularemia Occurring in Laboratory Workers.—LAKE and FRANCIS (*Public Health Reports*, 1922, **37**, 392) report on 6 cases of laboratory infection occurring in laboratory workers. Their paper is summarized as follows: All of the persons (6) who have been intimately engaged in the past two years in the laboratory in handling or dissecting rodents infected with the Utah strains of tularense have suffered an attack of tularemia. The diagnosis in each of the 6 cases rests upon the occurrence of a febrile period lasting about three weeks, positive serum reactions for agglutination and complement-fixation to antigens composed of Bacterium tularense and the absence of febrile attacks in 100 other persons in the laboratory coming in casual contact with infected rodents. Consideration must be given to the skin of the hands as a possible portal of entry of the infection in laboratory workers even in the absence of local lesion or lympha-

denitis. A second attack has recently occurred in Case I of the above series, two years and five months after his first attack. The second attack was associated with evident cracks on the fingers, on one of which there developed an inflammatory papule which was soon followed enlarged, painful and tender lymph nodes in the epitrochlear and axillary regions of the corresponding side, but without fever or other constitutional disturbance. Bacterium tularense was isolated from the papule by guinea-pig inoculation. The absence of constitutional symptoms in the second attack, although there was a local lesion and consequent lymphadenitis, is accounted for by the persistence of immune bodies acquired by the first attack. Unrecognized cases of tularemia probably occur in the known foci of infection in the United States, some of which may have febrile attacks without local lesions, while some may have local lesions and a secondary regional lymphadenitis without very notable constitutional disturbance. Routine serological tests for agglutination especially and for complement-fixation, using antigens composed of Bacterium tularense, would probably not only detect cases in known foci of infection but would bring to light unknown foci. Positive serological reactions are known to persist for two years after an attack. Light might be thrown upon the etiology of some fevers of undetermined origin. A warning is sounded against unwarranted indifference to an infection which in our experience has claimed all of those who have persistently worked with it in the laboratory.

The Serological Grouping of Meningococcus Strains Isolated in New York City in 1921 and 1922.—EVANS (*Public Health Reports*, 1922, **37**, 1247) has studied the immunological relations of meningococci isolated from recent cases of meningitis and compared them with strains which prevailed a few years ago. It is shown that, judged by bacteriotropin reactions, there has been a marked shifting of grouping, with a tendency to increase among the unclassified strains.

The Delinquent.—LESLIE (*Public Health Reports*, 1922, **37**, 1297) calls attention to the great economic loss and suffering entailed by delinquents who become public charges in penal institutions. Work of certain American observers is reviewed and commented on. A plea is made for study of the situation and for reshaping of the policy of the community in dealing with mentally deficient actual and potential criminals. The public-health bearings are especially brought out in connection with prostitution and venereal disease.

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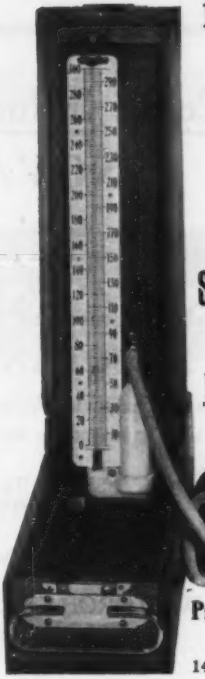

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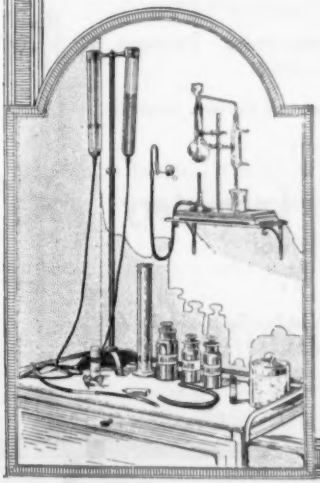

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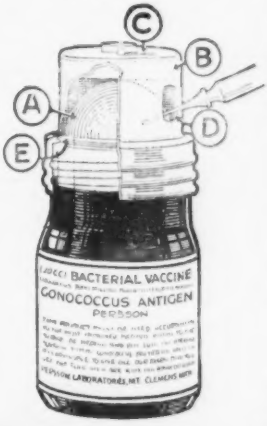

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